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A QUANTITATIVE STUDY OF THE FETAL GROWTH CHANGES IN THE PARTS OF THE HUMAN STOMACH WALL

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BY

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GROWTH OF CRYPTS AND GLANDS OF THE HUMAN STOMACH *

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MINNEAPOLIS

I. INTRODUCTION

The prenatal and postnatal changes in the mass and in the capacity of the stomach have been studied in some detail, and the qualitative changes in its musculature are well described. There is, however, almost no information on the quantitative changes in the gastric mucosa in the developmental period, although the applications of such data to gastric physiology in infancy and in childhood are obvious.

The present paper is a report of a quantitative study of one phase of this subject, namely, the growth in number of the gastric crypts and glands in later fetal life, infancy, childhood and adolescence. To this have been added data on the number of these structures in maturity, which were collected as a check on the findings for the developmental period. It is hoped to extend these studies later to a consideration of the dimensional changes of the gastric glands, to the modifications in their finer structure, and to a more detailed consideration of the relations of these findings to various physiologic interpretations of gastric function in the developmental period.

II. MATERIAL AND METHODS

The bulk of the material used in this study was obtained from necropsies of infants and children, which were conducted by the Department of Pathology of the University of Minnesota. The adult material came from the necropsies performed at the University Hospital. In all, forty-five stomachs were examined, but eleven were rejected because of pathologic findings or because of suspicious clinical histories. Table 1 summarizes this material.

The fixation of the material was kept as nearly uniform as possible, Zenker's acetic acid fixative being used in every instance. It sometimes happened that specimens coming from necropsy were temporarily placed in a strong formaldehyd solution, but these stomachs were washed at once and placed in Zenker's solution. The stomachs of the fetuses,

* From the Department of Anatomy, University of Minnesota.

new-born infants and older infants were fixed in toto. A piece of tissue from 5 to 10 sq. cm. was taken from each adult stomach and fixed in Zenker's fluid. The remainder of the viscus was placed in formaldehyd and later transferred to a 75 per cent. alcohol solution. The material was left in Zenker's fluid for twenty-four hours, washed in running water for twenty-four hours, and then placed in a 75 per cent. alcohol solution; this treatment reduced shrinkage to a minimum. Material to be sectioned was dehydrated, cleared and embedded in paraffin, according to the usual technic.

TABLE 1.—*Summary of Material*

Calculated or Observed Age	Case Number	Sex*	Crown-Heel Length	Sitting Height	Body Weight, in Kg.	Length of Life	Area of Gastric Mucosa in Sq. Cm.	Volume of Stomach in C.c. of Water Displaced
8.11 fetal months.....	19	♀	41	29.3	1.400	0	19.66	3.10
8.16 fetal months.....	11	♀	41.3	27.7	1.255	9 d.	30.58	7.50
8.20 fetal months.....	37	♂	44	31.5	2.205	11 d.	31.58	5.59
8.90 fetal months.....	33	♂	45	31	1.610	0	33.91	5.25
9.04 fetal months.....	24	♂	45.7	32	1.780	0	32.13	4.50
9.10 fetal months.....	34	♀	46	33	2.395	12 h.	31.08	6.25
9.37 fetal months.....	31	♀	47.5	33	2.946	5 h.	33.19	6.55
New-born.....	1	♀	48	31.5	2.900	6 d.	.....	5.50
New-born.....	2	♂	54	38	3.330	0	34.85	13.10
New-born.....	3	♀	50.5	35.5	3.370	0	27.38	7.55
New born.....	4	♂	48	32	3.500	1 d.	35.35	7.55
New-born.....	5	♂	52	36	3.680	0	35.78	4.50
New-born.....	6	♂	49.5	33	3.000	0	41.66	6.00
New-born.....	7	♀	52	34	3.050	0	38.75	11.00
New-born.....	8	♂	52	32	3.400	0	46.91	14.50
New-born.....	9	♂	51	34	3.360	0	45.25	12.10
New-born.....	10	♀	52	34	3.450	0	78.14	15.00
New-born.....	12	♂	54	37.5	3.350	24 h.	39.99	8.10
New-born.....	13	♂	53	36.5	3.230	8 h.	32.51	6.00
New-born.....	15	♂	52	35	2.570	0	39.58	7.00
New-born.....	25	♀	52	35	3.135	9 d.	34.41	16.20
2 months.....	22	♂	49	32.3	3.500	..	113.33	14.60
2 months.....	28	♂	64	43	5.892	..	162.35	21.00
5.5 months.....	21	♂	70	45	5.708	..	159.58	41.00
7 months.....	14	♂	68	46	5.550	..	168.16	25.00
17 months.....	30	♂	82	55	12.000†	..	213.41	42.00
22 months.....	39	♀	87	55	16.000†	..	167.58	40.00
2 years.....	43	♀	88	..	16.000†	..	230.91	44.45
3 years.....	27	♀	92	..	14.000†	..	154.33	46.00
3.5 years.....	32	♀	99	..	16.000†	..	.....	.....
6.5 years.....	29	♂	115	..	.....	..	258.16	85.25
15 years.....	42	♂	139	..	32.000†	..	657.91	247.83
23 years.....	41	♀	160	..	41.000†	..	543.50	230.50
39 years.....	38	♂	171	..	77.000†	..	542.08	234.50
44 years.....	26	♀	...	..	.....	..	470.66	102.75

* In this column, ♀ indicates female; ♂, male.
† Estimated.

The sections for the gland counts were cut at 15 microns, mounted serially, stained in Mallory's connective tissue stain, dehydrated, and cleared and mounted in balsam. Pieces of the stomach with the mucosal surface as nearly flat as was possible to obtain were used in this part of the work. The sections were cut in a plane parallel to the surface of the mucosa, thus presenting the glands in cross section.

Counts of the gastric crypts and glands were made of fifty different areas of 1 sq. mm. for each individual stomach. The counts were made seriatim, aside from the selection necessitated by the irregularities in the surface contour of the gastric mucosa.

The gastric crypts were counted directly from the mucosal surface of the stomach at a magnification of 16 diameters. The crypts were easily discerned under strong oblique illumination. The counts were made with a square representing 1 sq. mm., at a magnification of 16 diameters, ruled off on a coverslip and subdivided into sixteen minor squares. This was placed on the ocular diaphragm of the microscope used in making the counts.

The determination of the surface area of the gastric mucosa presents rather a difficult problem. After trying several methods, the following one was adopted. The stomach was divided in halves by splitting it along the greater and lesser curvatures, and a plaster cast was made of the mucosal surface. Thin tissue paper was then placed on the cast, moistened with water, molded carefully over the surface irregularities and allowed to dry. The tissue paper was then removed from the cast, flattened, and the outlines traced on standard thickness paper which was weighed. Having the total weight of the paper and its known weight per square centimeter, the surface area was easily calculated. This method eliminates the error caused by stretching the stomach in an attempt to reduce it to a flat surface.

III. LITERATURE

The development of the gastric crypts and glands has been a subject of some dispute among embryologists. Kölliker [1] believed the gastric crypts and glands were formed from thickened epithelial processes, which later became hollowed and grew downward into the mesenchyma. Laskowsky [2] thought the fundic glands were formed from invaginated cylindric epithelial cells through changes in their form. Schenk [3] accepts the explanation offered by Laskowsky in its entirety. Wolffhügel [4] gives some information concerning the histologic structure of the fundic glands in older rabbit embryos and in the new-born dog. Brand [5] accepted the views of Laskowsky and Schenk, but considered the connective tissue layer as the causative factor in the process of invagination. He thought that the glands originated from a large number of papillae of mucosal epithelium, which were marked out by the growth of the underlying mesenchyma. In this concept, the part played by the epithelium in the

1. Kölliker, A.: Entwickelungsgeschichte des Menschen und der höheren Thiere, Leipzig, 1861.

2. Laskowsky: Ueber die Entwickelung der Magenwand, Sitzungsb. d. k. Akad. d. Wissensch. Wein. **58**:137, 1868.

3. Schenk: Lehrbuch der vergleichenden Embryologie der Wirbelthiere, Ed. I, Wein, 1874.

4. Wolffhügel, G.: Ueber die Magenschleimhaut neugeborener Saügethiere, Ztschr. f. Biol. **12**:217, 1876.

5. Brand: Beiträge zur Entwickelung der Magen- und Darmwand, Verhandl. d. phys.- med. Gesellsch. zu Würzb. **9**:243, 1877.

origin of the glands is limited to the production of material for the gland cells. Later, Kölliker [6] confirmed and agreed with Brand in this explanation.

Sewall [7] believed the glands were primarily epithelial in origin, but that the chief and parietal cells were later replaced by cells of a mesenchymal origin.

Until Toldt's [8] work, the interest in the development of the gastric glands was limited chiefly to the method of their formation, and comparatively few observations were made on the actual details of their further development. This author, working on cat, pig and human material, decided that the glands and crypts were epithelial in origin and formed by downgrowths of the epithelium.

Johnson [9] described the gastric crypts as originating from vacuoles and pit-like depressions which first appeared in the epithelium on the side of the viscus proximal to the bursa omentalis. These pits increase in number in older embryos and become elongated, rounded or groove-like. The epithelial growth takes place both by the enlargement of the pits already formed and by the addition of new ones. The gastric glands first appear in embryos of 120 mm. as knoblike outgrowths from the bottoms of the crypts. For the most part, these are simple tubular glands, rarely branching, and varying considerably in length and diameter. In the older embryos, the glands become longer and more branched, their growth being more rapid than the growth of the crypts. At birth, the histologic structure is similar to that of the adult. Gundobin,[10] however, states that the glands do not reach the typical adult histologic structure until after the first year.

There is little published information on the number of glands per unit area of gastric mucosa or on the total number of glands in the stomach. Frey [11] estimated as many as 1,894 glands per square millimeter, in the pyloric region of the rabbit's stomach. Sappey [12] counted from 100 to 150 gastric crypts on the smaller papillae (gastric areas) of the mucosa, while the larger papillae gave counts ranging from 600 to 800 crypts, but these observations do not give a concrete expression of

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6. Kölliker, A.: Entwickelungsgeschichte des Menschen und der höheren Thiere, Leipzig, 1879.

7. Sewall: The Development and Regeneration of the Gastric Glandular Epithelium During Fetal Life and After Birth, J. Physiol. **1**:321, 1879.

8. Toldt, C.: Die Entwickelung und Ausbildung der Drüsen des Magens, Sitz. d. k. Akad. der Wissensch. Wein **82**, 1880.

9. Johnson, F. P.: The Development of the Mucous Membrane of the Esophagus, Stomach and Small Intestine in the Human Embryo, Am. J. Anat. **10**:521, 1910.

10. Gundobin, A. P.: Die Besonderheiten des Kindesalters, Berlin, 1912, p. 264, et seq.

11. Frey, H.: Handbuch der Histologie und Histochemie, 1874.

12. Sappey, Ph. C.: Traité d'anatomie descriptive, Ed. 4, Paris, 1889.

crypts per unit area. Sappey considered each crypt a true gland, not as an orifice of a number of glands.

Toldt [8] was the first investigator to determine the number of crypts and glands per unit area of human gastric mucosa. By multiplying this value by the total area of the gastric mucosa, he arrived at an estimate of the total number of glands in the stomach. He hardened the organ by placing it in 80 per cent. alcohol for eight days, then cut it in halves by incisions along the greater and lesser curvatures and spread it flat on a glass plate. The outline was then marked off, and the area calculated with an Amsler planimeter. To count the number of glands, Toldt made permanent preparations cut in such a manner that the glands were seen in cross section. The total number of glands in a given field were counted, and the total number of glands in the stomach were estimated by multiplying the area of the mucosa by the

TABLE 2.—*Toldt's Table*

Age of Person	Area of the Gastric Mucosa in Sq. Mm.	Per Sq. Mm.		Total Number of	
		Gastric Crypts	Gastric Glands	Gastric Crypts	Gastric Glands
Female embryo, end of the eighth (lunar) month (length of body, 39.5 cm.)	2,302	56	404	128,912	930,008
Female embryo, middle of the tenth (lunar) month (length of body, 47.5 cm.)	5,330	50	382	266,500	2,036,060
Stillborn mature male infant (body length, 50 cm.)	5,270	51	371	268,770	1,955,170
Girl, aged 10 years	50,510	56	336	2,828,560	16,971,360
Girl, aged 15 years	65,770	67	341	4,406,590	22,427,570
Man, aged 30	76,300	89	330	6,790,700	25,179,000

average number of glands per square millimeter. The author gives no more details as to his method of counting or as to the number of counts made.

Toldt's table for the increase in number of the gastric crypts and glands is shown in Table 2.

From Table 2 Toldt estimates that the number of gastric crypts increases about fifty-two fold from the ninth fetal month to maturity, while the number of glands only increases in the neighborhood of twenty-seven fold, in the same period. The gastric crypts increase about twenty-five times and the glands twelve times between birth and maturity. In the first ten years the number of crypts increased about eleven fold and the number of glands increased nine fold. According to Toldt's figures, the relation of the crypts to the glands is not changed in the last two months of prenatal life. The average number of glands to each crypt at birth is about seven, in later childhood about six, at fifteen years, five, and in maturity also about five. In the last two months of fetal life the increase in the number of glands is quite large, so that during this period they reach the peak in number per unit area.

After this period, there is no constant relation between the number of gastric crypts and the number of gastric glands.

IV. SUMMARY OF FINDINGS AND COMMENT

The Growth of Gastric Crypts and Glands per Unit Area of the Stomach.—The Gastric Crypts: The gastric crypts (foveolae gastricae) are small pit-like depressions in the mucosa, having at birth an average

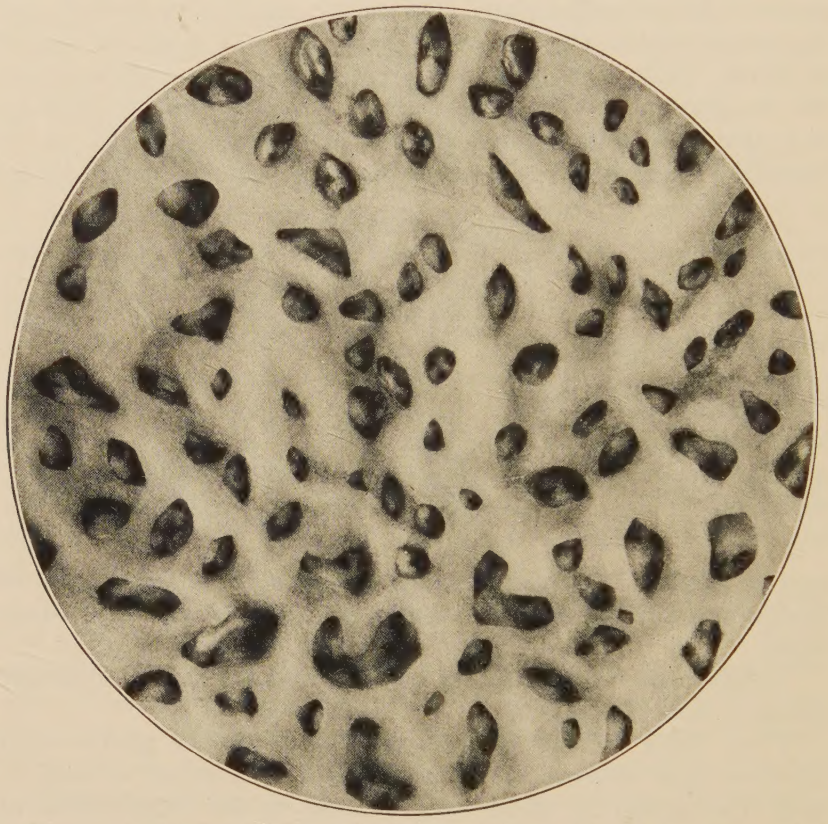

Fig. 1.—A drawing of the surface view of the gastric mucosa of a typical full-term, new-born infant.

depth of 0.108 mm. and an average width of 0.02 to 0.048 mm. (Johnson[9]). At their lower end they receive the openings or mouths of one or more gastric glands (glandulae gastricae propriae). These ostia vary in form, some being elongate, some circular and others groove-like. Their distribution over a given area of gastric mucous membrane is quite constant. When one finds an unusually large crypt, as a rule there are several small ones crowded about it. In the fetuses of the ninth and tenth months they are distinctly larger than in the new-born,

and there is a correspondingly smaller number per square millimeter. Figure 1 is a surface view of a typical area of the new-born gastric mucosa at a magnification of approximately 66 diameters.

Table 3 shows the average number of crypts per square millimeter in fetuses of the ninth and tenth months,[13] as determined by counts on

TABLE 3.—*Number of Crypts in the Stomachs of the Fetuses of the Ninth and Tenth Months*

Number	Calculated Age in Fetal Months	Area of Gastric Mucosa in Sq. Cm.	Average Number of Gastric Crypts per Sq. Mm.	Estimated Total Number of Crypts
19	8.11	19.66	32.14	63,206
11	8.16	30.58	32.08	98,110
37	8.20	31.58	32.46	102,518
33	8.90	33.91	35.48	120,333
Average	8.34	28.93	33.04	96,041
24	9.04	32.13	41.26	132,601
34	9.10	31.08	42.52	132,181
31	9.37	33.19	45.80	152,023
Average	9.17	32.13	43.19	138,935

TABLE 4.—*Range, Interquartile Range and Semi-Interquartile Range Calculated from the Raw Data on the Number of Gastric Crypts Per Square Millimeter*

Number	Age	Average Number of Crypts per Sq. Mm.	Minimum Number	Maximum Number	Total Range	Interquartile Range	Semi-interquartile Range
19	8.11 fetal months	32.14	27	38	11	2	1
11	8.16 fetal months	32.08	27	42	15	2	1
37	8.20 fetal months	32.46	26	38	12	2.5	1.25
33	8.90 fetal months	35.48	30	41	11	1.5	0.75
24	9.04 fetal months	41.26	35	50	15	2	1
34	9.10 fetal months	42.52	36	49	13	2.5	1.25
31	9.37 fetal months	45.80	38	53	15	2.5	1.25
9*	Birth	49.46	40	60	20	2	1
22	2 months	50.21	42	59	17	3	1.5
28	2 months	50.16	40	60	20	3	1.5
21	5.5 months	53.80	48	62	14	2	1
14	7 months	54.06	45	61	16	2	1
30	17 months	64.98	50	75	25	2.5	1.25
39	22 months	67.86	60	82	22	1.5	0.75
43	2 years	65.98	60	73	13	2	1
27	3 years	66.40	58	72	14	2	1
32	3.5 years	66.08	58	74	16	2	1
29	6.5 years	65.60	53	81	28	2	1
42	15 years	61.98	54	77	23	1.5	0.75
41	23 years	60.56	53	70	17	2	1
38	39 years	62.12	57	71	14	2	1
26	44 years	62.84	55	73	18	2.5	1.25

* Case 9 of the new-born series is taken as a typical specimen from this series.

seven specimens. Each average is based on counts of fifty different areas from each stomach. These averages rise from 32.14 crypts per square millimeter at 8.11 months to 35.48 at 8.9 months and 45.80 at 9.37 months. Thus there is an increase of nearly one-half in the number of crypts per unit area between the beginning of the ninth and

13. The estimates of the ages of these specimens were made with the aid of the empirical formula for determining fetal age developed by Scammon and Calkins: Proc. Soc. Exp. Biol. & Med. **20**:353, 1923.

the middle of the tenth lunar month. The most marked increase seems to be in the latter part of the ninth and the early part of the tenth month. The variability of the number of crypts per square millimeter in individual specimens in the fetal period is not very great. It is illustrated by the frequency curves shown in Figure 2 and by the

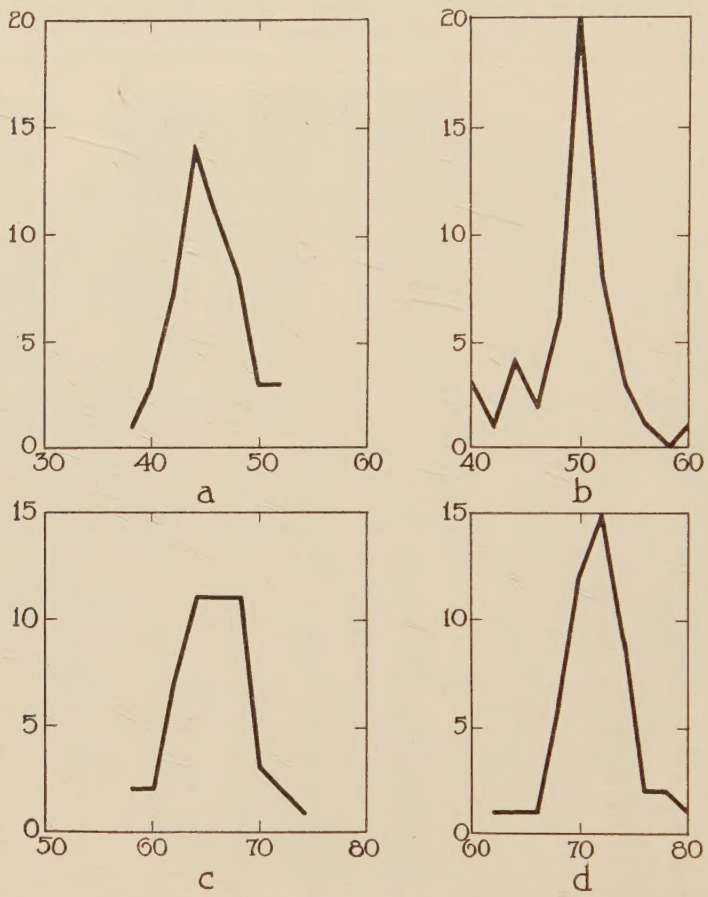

Fig. 2.—Four point-to-point frequency curves each showing the distribution of fifty observations on the number of gastric crypts per square millimeter. Ordinates: number of observations at given values. Abscissas: number of gastric crypts per square millimeter; *a*, fetus of 9.37 months, calculated age; *b*, typical full-term new-born infant; *c*, child aged 3½ years; *d*, adult, aged 23.

values for the total and the semi-interquartile ranges included in Table 4.

The average number of crypts per square millimeter in the full-term new-born infant is 50.24, the probable error of the mean being ± 0.16. The average is based on a total of 700 sq. mm. counts, fifty on each of fourteen specimens. The variability in the number of crypts

per area is somewhat greater than in the fetal material, the standard deviations of the various specimens ranging from 3.95 to 10.82 with an average of 6.08 crypts, and the coefficients of variability ranging from 7.90 to 21.64 with an average of 12.17 per cent. The standard deviation of the entire group of 700 counts is 6.39 crypts, the probable error of the standard deviation being ± 0.16, and the coefficient of variability is 12.78 per cent., the probable error of the coefficient of variability being ± 0.12. Figure 3 is a frequency curve illustrating the distribution of the entire group of 700 counts; Table 5 gives the average count for each specimen with measures of its variability.

The number of crypts per unit area remains fairly constant from birth until some time between the first and the third postnatal months.[14] But between the fifth and sixth months there is evidence of a slight increase in number, the average count at 5½ months being 53.80 per

TABLE 5.—*Range, Standard Deviation, Coefficient of Variability of the Number of Gastric Crypts Per Square Millimeter in the New-Born Infants*

Number	Average	Minimum Number	Maximum Number	Total Range	Standard Deviation	Coefficient of Variability
1	50.70	38	64	26	5.82	11.64
2	50.42	32	82	50	7.67	15.35
3	50.36	38	65	27	5.45	10.89
4	50.06	32	96	64	10.82	21.64
5	50.94	38	82	44	9.70	19.41
6	50.27	39	65	26	6.25	12.50
7	50.76	33	64	31	6.06	12.12
8	49.80	38	63	25	5.33	10.65
9	49.46	40	60	20	3.95	7.90
10	49.54	38	61	23	4.70	9.40
12	49.80	36	59	23	4.72	9.45
13	50.42	40	62	22	5.14	10.29
15	50.18	38	63	25	4.06	8.12
25	50.78	39	71	32	5.51	11.02
Average.....	50.24	..	..	31.3	6.08	12.17

square millimeter. The count is only slightly greater at 7 months but increases approximately one-fifth, to about 65 crypts per square millimeter at 17 months. The average count for the second year is about 66, and it remains almost constant up to 6½ years. No specimens between 6½ and 15 years were available for study. The count at the latter age was approximately 62 crypts per square millimeter; this value, with very slight variations, seems to be typical of the adult stomach.

In summarizing, it may be said that the present data indicate that the number of crypts per unit area of gastric mucosa increases rapidly in the last months of fetal life to birth. It apparently remains constant during the first trimester of postnatal life and then enters on another period of increase which is concluded toward the end of the second year, when the maximum number of crypts per unit area is reached. This

14. One of the two specimens of this period was premature. This factor affected the surface area of the stomach but not the number of crypts per square millimeter.

number remains practically unchanged until middle childhood, but is eventually followed by a slight decrease (the exact date of which is unknown) before adolescence, when the adult number of crypts per unit area is attained.

Tables 6 and 7 and Figure 4 show these changes in more detail. Figure 5 represents a series of camera lucida tracings of 1 sq. mm.

Fig. 3.—A point-to-point frequency curve showing the distribution of 700 observations on the number of gastric crypts per square millimeter in fourteen new-born infants. Ordinates: number of observations at given values. Abscissas: number of gastric crypts per square millimeter.

areas of the gastric mucosa at different ages, drawn at a standard magnification.

The Gastric Glands: The gastric glands (glandulae gastricae propriae) tend to follow the same course of development as do the gastric crypts. In the new-born, they average 0.255 mm. in length and

TABLE 6.—*Number of Crypts in the Stomachs of Fourteen Full-Term New-Born Infants*

Number	Area of Gastric Mucosa in Sq. Cm.	Average Number of Gastric Crypts per Sq. Mm.	Estimated Total Number of Crypts
1*	.....	50.70	.....
2	34.85	50.42	175,713
3	27.38	50.36	137,900
4	35.35	50.06	177,002
5	35.78	50.94	182,278
6	41.66	50.27	209,454
7	38.75	50.76	196,695
8	46.91	49.80	233,641
9	45.25	49.46	223,846
10	78.14	49.54	387,110
12	39.99	49.80	199,155
13	32.51	50.42	163,945
15	39.58	50.18	198,627
25	34.41	50.78	174,764
Average	40.81	50.24	204,625

* The area of the mucosa and the total number of crypts in Case 1 is omitted, as it was impossible to obtain an accurate estimate of the surface area of this stomach.

TABLE 7.—*Number of Crypts in the Stomach in Postnatal Life*

Number	Age	Area of Gastric Mucosa in Sq. Cm.	Average Number of Gastric Crypts per Sq. Mm.	Estimated Total Number of Crypts
22	2 months	113.33	50.21	569,046
28	2 months	162.35	50.16	814,347
Average	2 months	137.84	50.18	691,696
21	5.5 months	159.58	53.80	858,558
14	7 months	168.16	54.06	909,108
Average	6.25 months	163.87	53.93	883,833
30	17 months	213.41	64.98	1,386,781
39	22 months	167.58	67.86	1,137,220
43	2 years	230.91	65.98	1,323,587
Average	21 months	203.97	66.27	1,282,529
27	3 years	154.33	66.40	1,024,773
32*	3.5 years	.....	66.08	.....
Average	3.25 years	154.33	66.24	1,024,773
29	6.5 years	258.16	65.60	1,693,831
Average	6.5 years	258.16	65.60	1,693,831
42	15 years	657.91	61.98	4,077,763
41	23 years	543.50	60.56	3,291,436
38	39 years	542.08	62.12	3,367,421
26	44 years	470.66	62.84	2,957,668
Average	30.25 years	553.54	61.87	3,423,572

* The total number of crypts and the total area of the gastric mucosa in Case 32 is omitted, since only a small piece of this stomach was saved at necropsy.

0.048 mm. in diameter at the neck (Johnson[9]). The accounts given by various workers in regard to the size of the adult glands are quite different. Gegenbaur[15] describes them as being 0.6 mm. in length, partially simple and partially compound in structure. Piersol[16] states that their length is from 0.4 to 2 mm., and that the diameter of the secreting tubule is from 0.002 to 0.007 mm. Testut[17] finds that as many as eight to twelve glands open into a single crypt. Kölliker[18] gives the dimensions as 0.2, 0.75 or even 1 mm. in length and 0.02, 0.26 and 0.036 mm. in diameter. Frey[11] describes the glands as being about 1.13 mm. in length and from 0.0564 to 0.0451 mm. in diameter.

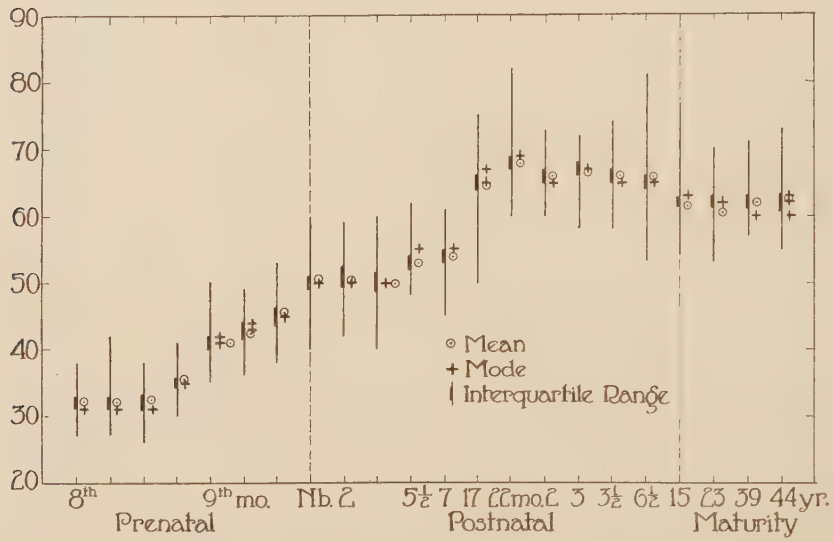

Fig. 4.—A graph showing the range, mean, mode and interquartile range of the entire series of observations on the number of gastric crypts per square millimeter, made in this study. Ordinates: number of gastric crypts per square millimeter. Base line: ages of persons.

According to Frey, the glands are much shorter and of smaller caliber in children. Four, five, six or seven glands may arise from a single crypt.

Table 8 gives the results of the gland counts in the fetuses of the ninth and tenth months; averages for the different ages are derived from fifty counts in each instance. The glands show the same steady increase per unit area evidenced by the crypts for this age. In the fetus of 8.11 months the average number was 77.72 glands per square millimeter

15. Gegenbaur, C.: Lehrbuch der Anatomie des Menschen, Ed. 5, Leipzig **2**:55, 1892.
16. Piersol, G. A.: Human Anatomy, Philadelphia **2**:1621, 1908.
17. Testut, L.: Traité d'anatomie humaine, Paris **4**:133, 1912.
18. Kölliker, A.: Mikroskopische Anatomie **2**:199, 1852.

and the fetus of 8.90 months showed 84.08 glands per square millimeter. The increase is more rapid in the first third of the tenth month than at any other period in the two fetal months studied. In the fetus of 9.04 months the average number of glands per unit area was 92.10 and in the fetus of 9.37 months was 113.36. This corresponds roughly to the rapid increment in the number of gastric crypts per unit area dur-

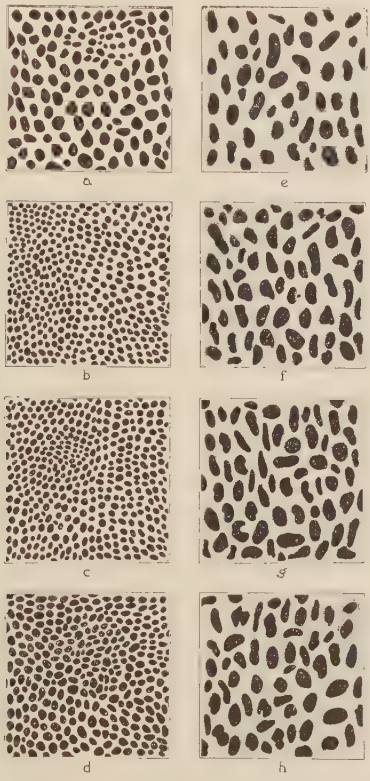

Fig. 5.—*a, b, c, d,* projection drawings of 1 square millimeter areas of frontal sections of gastric mucosa. The black areas represent cross sections of the glands; *e, f, g, h,* camera lucida drawings of 1 square millimeter surfaces of gastric mucosa. The black areas represent the crypts; *a, e,* mucosa of a typical full-term new-born infant; *b, f,* mucosa at 2 years; *c, g,* mucosa at 6½ years; *d, h,* mucosa at maturity. Magnification, 47 diameters.

ing this period. The variation in the range of the observations from which these averages were calculated is illustrated in Table 10 and Figure 6.

In the new-born infant, the number of glands is practically the same in relation to the number of crypts as in the ninth and tenth fetal months. In the 700 areas counted in the fourteen stomachs of the new-born series (50 sq. mm. for each stomach), the average number

of glands per square millimeter was 121.36. The variation in the averages for the individual cases was less than five glands per square millimeter, ranging from 119.72 to 123.22. The range for this entire series was from 90 to 154 glands per square millimeter (Figs. 7 and 8).

There was no apparent increase in the number of glands in the new-born infants who had ingested food. Some of these had lived for several days and, so far as could be determined, they were in no way different from stillborn infants. The averages for the individual specimens are given in Table 9.

TABLE 8.—*Number of Glands in Stomachs of the Fetuses of the Ninth and Tenth Months*

Number	Calculated Age in Fetal Months	Area of Gastric Mucosa in Sq. Cm.	Average Number of Gastric Glands per Sq. Mm.	Estimated Total Number of Glands
19.	8.11	19.66	77.72	152,844
11	8.16	30.58	78.62	240,443
37	8.20	31.58	78.18	246,915
33	8.90	33.91	84.08	285,165
Average	8.34	28.93	79.65	231,341
24	9.04	32.13	92.10	295,990
34	9.10	31.08	108.10	336,050
31	9.37	33.19	113.36	376,275
Average	9.17	32.13	104.52	336,105

TABLE 9.—*The Estimated Total Number of Glands in the Stomachs of Fourteen New-Born Infants*

Number	Area of Gastric Mucosa in Sq. Cm.	Average Number of Gastric Glands per Sq. Mm.	Estimated Total Number of Glands
1	.....	122.12	.....
2	34.85	120.54	420,081
3	27.38	120.76	330,677
4	35.35	121.10	428,185
5	35.78	121.22	433,761
6	41.66	121.66	506,908
7	38.75	122.36	474,145
8	46.91	123.22	578,098
9	45.25	122.40	553,957
10	71.84	120.68	866,977
12	39.99	121.34	485,250
13	32.51	119.72	389,281
15	39.58	120.58	477,291
25	34.41	121.46	418,016
Average	40.81	121.36	489,432

It appears from an examination of Table 11 that the development of the glands in number *per given area* is temporarily retarded from birth until the age of 2 months, there being only a very small increase during this time in the average number of glands per square millimeter. At birth, the average number of glands is 121.36 and at two postnatal months it is only slightly higher (128.28 glands per square millimeter). Between 2 and 5½ months the average number of glands per square millimeter is increased to about 181. Between the ages of

7 and 17 months there is an enormous growth in the number of glands per given area, the increment being about 225 per cent. The glands found at these ages and to the age of 6½ years are much smaller in caliber than they are at earlier and later periods, the mucosal connective tissue is practically obliterated and the glands are packed together very closely. It is during these years of childhood that the peak in number of glands per given area is reached (Tables 10 and 11 and Fig. 6).

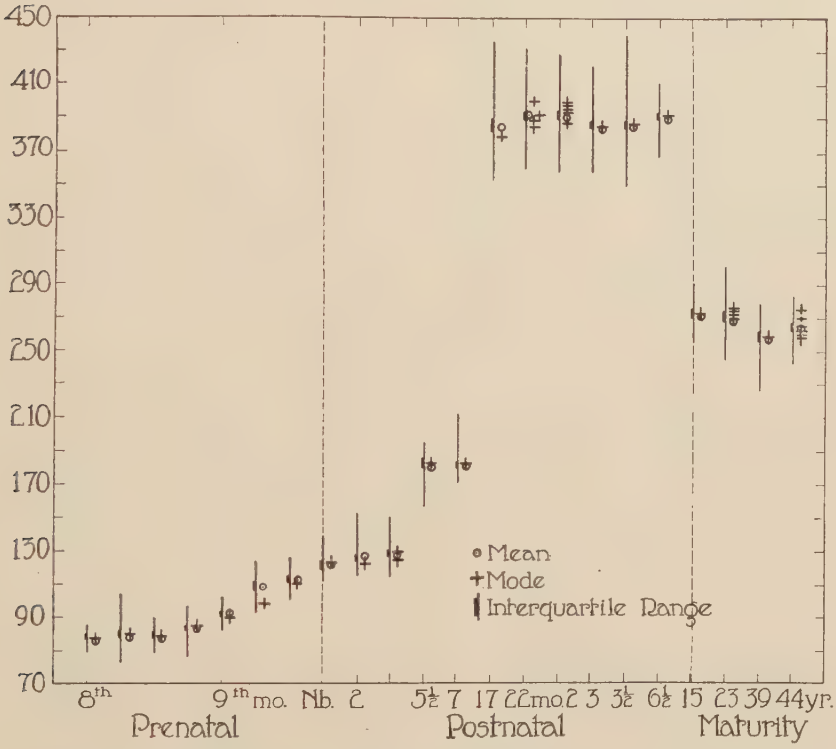

Fig. 6.—A graph showing the range, mean, mode and interquartile range of the entire series of observations made on the number of gastric glands per square millimeter. Ordinates: number of gastric glands per square millimeter. Base line: ages of persons.

From the age of 6½ to 15 years, the number of glands per square millimeter shows a decrease of nearly one-third. The exact time at which this decrease takes place has not been accurately determined, but it is evident that the major portion has occurred before 15 years, although the adult stomachs seem to show a slight decrease from the number found in the adolescent. It is possible that the variation shown in the last two adult specimens (Cases 38 and 26) in Table 11 indicates some further drop in numbers, but the relatively small amount of data at

TABLE 10.—*Range, Interquartile Range, Semi-Interquartile Range and Average Calculated from Raw Data on the Number of Gastric Glands Per Square Millimeter*

Number	Age	Average Number of Glands per Sq. Mm.	Minimum Number	Maximum Number	Total Range	Interquartile Range	Semi-interquartile Range
19	8.11 fetal months	77.72	70	85	15	3.0	1.5
11	8.16 fetal months	78.62	63	104	41	3.0	1.5
37	8.20 fetal months	78.62	69	89	20	3.0	1.5
33	8.90 fetal months	84.08	67	97	30	2.5	1.25
24	9.04 fetal months	92.10	82	102	20	2.5	1.25
34	9.10 fetal months	108.10	93	123	30	3.0	1.5
31	9.37 fetal months	113.36	101	126	25	4.0	2.0
9*	Birth	122.40	112	139	27	4.0	2.0
22	2 months	127.30	115	152	37	3.0	1.5
28	2 months	129.26	114	150	36	4.0	2.0
21	5.5 months	180.50	157	195	38	6.0	3.0
14	7 months	182.12	171	212	35	2.5	1.25
30	17 months	385.76	352	435	83	8.0	4.0
39	22 months	392.22	359	432	73	7.0	3.5
43	2 years	389.90	357	428	71	7.5	3.75
27	3 years	384.70	357	421	64	7.0	3.5
32	3.5 years	385.86	349	440	91	5.0	2.5
29	6.5 years	390.72	367	392	25	5.0	2.5
42	15 years	272.64	255	291	36	6.0	3.0
41	23 years	269.92	245	301	56	5.5	2.75
38	39 years	258.88	227	279	52	6.0	3.0
26	44 years	264.92	243	283	40	6.0	3.0

* Case 9 is taken as a typical specimen from the new-born series.

TABLE 11.—*Number of Glands in the Stomach in Postnatal Life*

Number	Age	Area of Gastric Mucosa in Sq. Cm.	Average Number of Gastric Glands per Sq. Mm.	Estimated Total Number of Glands
22	2 months	113.33	127.30	1,442,732
28	2 months	162.35	129.26	2,098,536
Average	2 months	137.84	128.28	1,770,634
21	5.5 months	159.58	180.50	2,880,478
14	7 months	168.16	182.12	3,062,639
Average	6.25 months	163.87	181.31	2,971,558
30	17 months	213.41	385.76	8,232,758
39	22 months	167.58	392.22	6,572,952
43	2 years	230.91	389.90	9,008,438
Average	21 months	203.97	389.29	7,936,382
27	3 years	154.33	384.70	5,927,202
32*	3.5 years	.....	385.86	.....
Average	3.25 years	154.33	385.28	5,937,202
29	6.5 years	258.16	390.72	10,087,085
Average	6.5 years	258.16	390.72	10,087,085
42	15 years	657.91	272.64	17,937,421
41	23 years	543.50	269.92	14,670,152
38	39 years	542.08	258.88	14,033,452
26	44 years	470.66	264.92	12,468,899
Average	30.25 years	553.54	266.59	14,774,481

* The total number of glands and the total area of the mucosa in Case 32 are omitted since only a small piece of this stomach was saved at necropsy.

hand hardly justifies an absolute statement on this subject. It is true, however, that the adults and the 15 year old specimen (Case 42) show more variation than do the stomachs of the preceding members of the series. This may be significant when one considers that there were more glands per square millimeter being counted in the stomachs of the younger persons, and hence the probability of error was larger. The glands in the adult have increased in size, the lumen is narrowed and the mucosal connective tissue is confined to thin sheets encircling each group

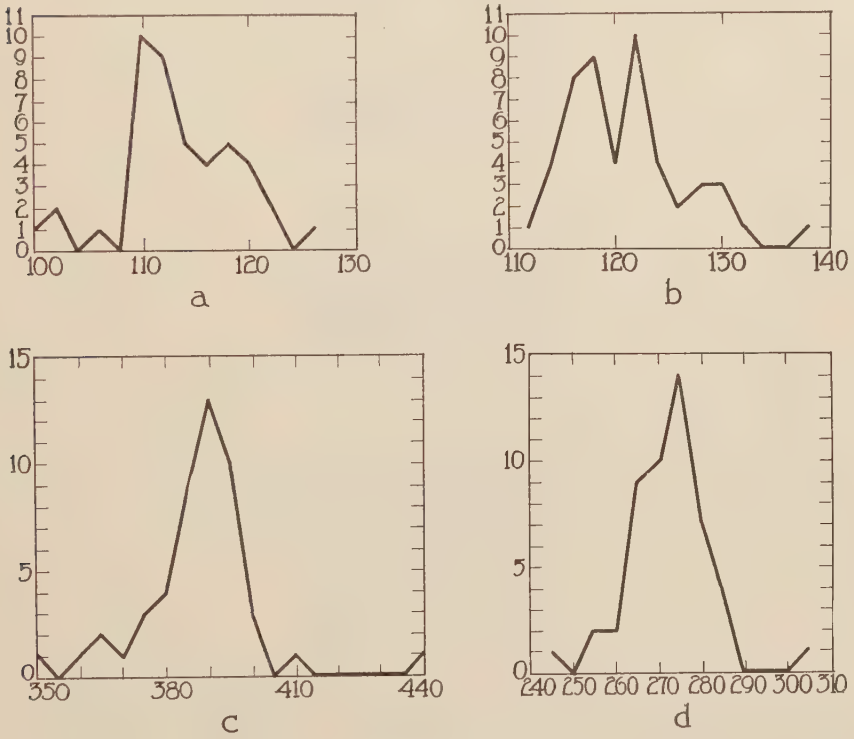

Fig. 7.—Four point-to-point frequency curves, each showing the distribution of fifty observations on the number of gastric glands per square millimeter. Ordinates: number of observations at given values. Abscissas: number of gastric glands per square millimeter; *a*, fetus of 9.37 months calculated age; *b*, typical full-term new-born infant; *c*, child aged 3½ years; *d*, adult, aged 23.

of glands and the membrana propria separating the individual elements. The glands have lengthened materially and are from two to three times larger than in early childhood. These changes are illustrated by Figure 9, which shows a series of vertical sections of the gastric mucosa at different ages.

Table 12, calculated from data given in Tables 8, 9 and 11, gives the number of gastric glands per crypt at the different ages studied. From

the ninth fetal month until the third month of postnatal life, the relation of about 2.5 glands per crypt is essentially the same. At 5½ and at 7 postnatal months, the number of glands per crypt is 3.35. From

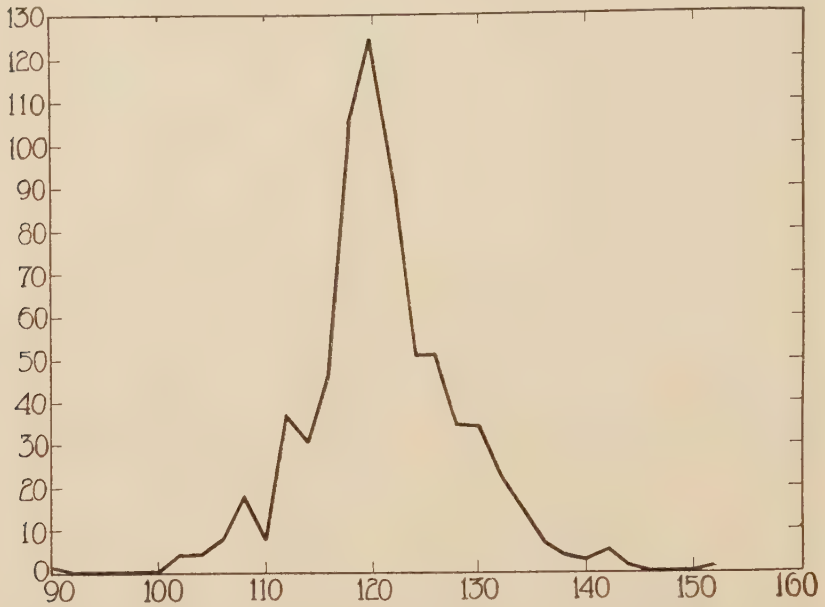

Fig. 8.—A point-to-point frequency curve showing the distribution of 700 observations on the number of gastric glands per square millimeter in fourteen new-born infants. Ordinates: number of observations at given values. Abscissas: number of gastric glands per square millimeter. Magnification, 60 diameters.

TABLE 12.—*Number of Gastric Glands per Gastric Crypt in the Individuals of Different Ages*

Age	Average Number of Crypts per Sq. Mm.	Average Number of Glands per Sq. Mm.	Average Number of Glands per Crypt
9 fetal months	33.04	79.65	2.41
10 fetal months	43.19	104.52	2.42
New-born	50.24	121.36	2.41
2 months	50.18	128.28	2.55
5.5 months	53.80	180.50	3.35
7 months	54.06	182.12	3.36
17 months	64.98	385.76	5.93
22 months	67.86	392.22	5.77
2 years	65.98	389.90	5.90
3 years	66.40	384.70	5.79
3.5 years	66.08	385.86	5.83
6.5 years	65.60	390.72	5.95
15 years	61.98	272.64	4.39
23 years	60.56	269.96	4.45
39 years	62.12	258.88	4.16
44 years	62.84	264.92	4.21

17 months to 6½ years the average is nearly six glands per crypt. In the older persons, namely, the 15 year old boy and the three adults, the average is about 4.3 glands per crypt.

B. GROWTH IN SURFACE AREA OF THE GASTRIC MUCOSA

Although this study was primarily concerned with the growth of both gastric crypts and glands, it was also necessary to calculate the surface area of the gastric mucosa at different ages, in order to estimate the total numbers of crypts and of glands in the viscus. This part of

Fig. 9.—A series of projection drawings of the epithelial and glandular elements of the gastric mucosa: *a*, typical full-term new-born infant; *b*, child, aged 2 years; *c*, child, aged 6½ years; *d*, mature individual.

the study brings out some interesting features, particularly in comparison with the results of other workers. The publications of Toldt,[8] of Lissenko [19] and of Dargein [20] contain all of the available published records on gastric area. These data were brought together by Scammon,[21]

19. Lissenko, W.: The Growth and Structure of the Stomach in Childhood, Dissert., St. Petersburg, 1899, quoted from review in Jahresb. f. Anat. **3**:1900, and from Gundobin, A. P.: Die Besonderheiten des Kindesalters, Berlin, 1912, p. 264.

20. Dargein, P.: Surface et volume comparés du l'estomac et du duodenum, Bibliog. Anat. **7**:207, 1899.

21. Scammon, R. E.: Some Graphs and Tables Illustrating the Growth of the Human Stomach, Am. J. Dis. Child. **17**:395 (June) 1919.

who analyzed them and presented them in tabular form. Table 13 contains the data compiled by Scammon, with the present series added thereto. It is interesting to note that the data of Lissenko and Dargein, although widely differing in actual figures, follow the same type of curve of growth (Scammon).

In the present series, the surface area of the mucosa shows a rather rapid increase from 28.93 sq. cm. at nine fetal months to 40.81 sq. cm.

TABLE 13.—*Area of the Gastric Mucosa in Square Centimeters**

Age	Area (in Sq. Cm.) of Gastric Mucosa According to			
	Present Series	Toldt	Lissenko	Dargein
8th fetal month	.....	23.02	.....	.....
9th fetal month	28.93	.....	.....	.....
10th fetal month	32.13	53.30	.....	.....
Birth	40.81	52.70	26.90	12.75
2 months	137.84	.....	60.20	31.00
3 to 3.5 months	.....	.....	67.70	48.00
5 to 5.5 months	159.58	.....	.....	55.00
6.5 to 7 months	168.16	.....	85.70	67.00
8 months	.....	.....	.....	82.00
9 months	.....	.....	125.70	.....
11 months	.....	.....	.....	118.00
1 year	.....	.....	133.90	.....
17 months	213.41	.....	.....	.....
22 months	167.58	.....	.....	.....
2 years	230.91	.....	.....	.....
3 years	154.33	.....	142.90	.....
6.5 years	258.16	.....	.....	.....
10 years	.....	505.10	.....	.....
15 years	657.91	657.70	.....	.....
Adult	518.74†	763.00	454.70	600.00

* The results obtained in this investigation are compared with the results of Toldt, Lissenko and Dargein.

† Average of three cases.

TABLE 14.—*Number of Times the Area of the Gastric Mucosa Increases from Different Ages to Maturity*

Age of the Individuals	Average Area of Gastric Mucosa in Sq. Cm.	Total Number of Times Increase to the Adult Period
9 fetal months	28.93	17.93
10 fetal months	32.13	16.14
New-born	40.81	12.71
2 months	137.84	3.76
5.5 months	159.58	3.25
7 months	168.16	3.08
17 months	213.41	2.43
22 months	167.58	3.09
2 years	230.91	2.24
3 years	154.33	3.36
6.5 years	258.16	2.00
15 years	657.91	—0.78
Adult	518.74	0.0

at birth. From birth to the third postnatal month the area increases nearly 3.5 times, rising from 40.81 sq. cm. to 137.84 sq. cm. After this period there appears to be a slow but steady growth until the seventeenth month, when the area is 213.41 sq. cm. Following this stage, the data fluctuate considerably but give evidence of a more or less steady increase.

Table 14 shows the number of times which the area of the gastric mucosa increases between the different ages in the developmental period and maturity. From the ninth fetal month to maturity there is an increase of nearly eighteen fold, from the tenth fetal month to maturity an increase of sixteen fold and from birth to maturity there is an increase of nearly thirteen fold. At 2 postnatal months this increase is nearly four fold, at 17 months it is 2.5 fold and at 6½ years it is but two fold.

Table 15 and Figure 10 show the number of times the area of the gastric mucosa increases from different ages to maturity as compared with the findings of Toldt,[8] of Lissenko [19] and of Dargein.[20] The absolute figures are quite at variance but all show the same general type of growth curve, as is indicated by the comparative histogram shown in Figure 10.

TABLE 15.—*Number of Times the Area of the Gastric Mucosa Increases from Different Ages to the Adult Period* *

Age	Number of Times Gastric Mucosa Increases from Each Age to Adult Period			
	Present Series	Toldt	Lissenko	Dargein
8th fetal month	.....	33.14	.....	.....
9th fetal month	17.93	.....	.....	.....
10th fetal month	16.14	14.31	.....	.....
Birth	12.71	14.47	16.90	47.05
2 months	3.76	.....	7.55	19.35
3 to 3.5 months	.....	.....	6.71	12.50
5 to 5.5 months	3.25	.....	.....	10.90
6.5 to 7 months	3.08	.....	5.30	8.95
8 months	.....	.....	.....	7.31
9 months	.....	.....	3.61	.....
11 months	.....	.....	.....	5.08
1 year	.....	.....	3.39	.....
17 months	2.43	.....	.....	.....
22 months	3.09	.....	.....	.....
2 years	2.24	.....	.....	.....
3 years	3.36	.....	3.18	.....
6.5 years	2.00	.....	.....	.....
10 years	.....	1.51	.....	.....
15 years	—0.78	1.16	.....	.....
Adult	0.00	0.00	0.00	0.00

* Results obtained in this study are compared with data from Toldt, Lissenko and Dargein.

C. GROWTH IN THE TOTAL NUMBER OF GASTRIC CRYPTS AND GLANDS

The Gastric Crypts: The total number of crypts and glands in the stomach may be estimated by multiplying the number per unit area by the total area of the gastric mucosa measured in terms of the same unit. In the fetus of 8.11 months, the total number of crypts so calculated was 63,206 and in the fetus of 9.37 months it was 152,023, an increment of nearly 250 per cent. The main factor causing the increase in the total number of crypts for this period is the rapid growth in the total area of the gastric mucosa, which expands fully one-third in this time. The total number of crypts in the stomach of the new-born seems to be controlled primarily by the area of the mucosa. This area is quite variable, ranging from 27.38 to 78.14 sq. cm. in the specimens studied. The

stomach measuring 78.14 sq. cm. was nearly twice as large as the others of the series, but in spite of this enormous variation in size, the number of crypts per unit area is very constant.

Surface area then *apparently* does not control the distribution of the crypts, as no constant difference in their number per given area was observed in any member of the series. In other words, contraction or expansion of the stomach wall does not influence the number of crypts per unit area of gastric wall. What probably happens when a stomach is moderately expanded is a smoothing out of the rugae into a flat surface but with no actual expansion or stretching of the epithelium or epithelial

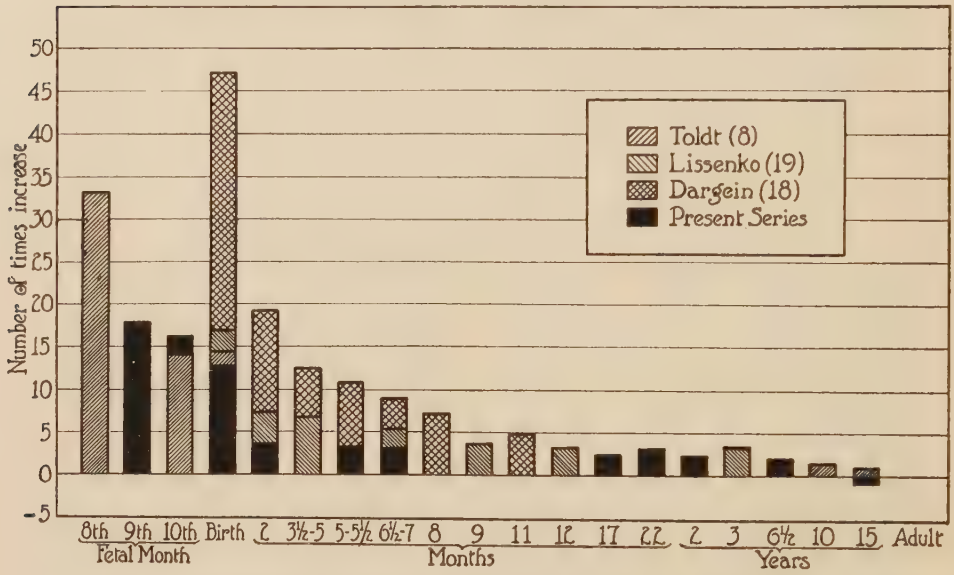

Fig. 10.—Comparative histogram, showing the number of times the area of the gastric mucosa increases from the eighth fetal month to maturity. Four sets of data are compared in this figure—that of Toldt, Lissenko, Dargein and the present series. Ordinates: number of times increase in the area of the gastric mucosa. Abscissas: ages of individuals.

bodies, the crypts or the glands. When the number of crypts per unit area is plotted against the area of the gastric mucosa in square centimeters, the result is nearly a horizontal line (Fig. 11), indicative of no correlation between these two factors. However, it is probable that hyperdistention of the stomach would change this relation. Experimental studies on this phase of the subject are now in progress.

It does not appear that the various parts of the stomach are in any way different with respect to the numbers of crypts. It is true that those present in the pylorus were somewhat more difficult to count accurately because of the villous processes in this region; when such

a count can be made it shows no marked departure from the average run of observations.

The average area of the mucosa in the neonatal series was 40.81 sq. cm.; the average total number of crypts 204,625. There was no apparent difference in the areas of the stomachs of the infants who had both lived and ingested food and those who were stillborn. By 2 months the total number of crypts has increased to an estimated number of 691,696 and at 5½ and 17 months this number is calculated to be 883,833. Between 17 months and 2 years the total number of crypts is calculated to be 1,282,529. From this period to 6½ years the total number of crypts is controlled primarily by the growth in surface area as no further increase occurs in their numbers per unit area.

By 6½ years, the total number of crypts has reached approximately 700,000. There is a steady increment in the total number of crypts

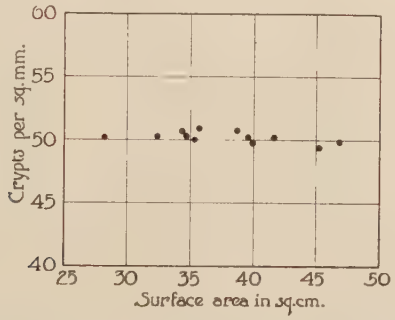

Fig. 11.—A field graph showing the relation between the surface area of the gastric mucosa and the number of crypts per square millimeter in the new-born series. Ordinates: number of crypts per square millimeter. Abscissas: surface area of the mucosa in square centimeters.

concomitant with the later increase in surface area of the mucosa. The slight increment in the number of crypts per unit area during infancy and early childhood apparently affects this to no great extent, although both factors must be considered as a part of the growth process. The total calculated number of crypts in Case 42, a boy, aged 15, is quite markedly higher than that of the adults studied, being 4,077,763. This case can only be explained on the basis of gratuitous variation, as this stomach was perfectly normal in every way. Scammon [21] has pointed out clearly the variability of the stomach in capacity and weight. The other three cases of this series seem to run more or less constant with regard to area. The large area of the mucosa in Case 42 makes the count of the total number of crypts for this stomach quite high. The average for the total calculated number of crypts in the three adult cases was 3,205,508.

The Gastric Glands: The rapid postnatal growth in number of gastric glands per unit area has a more profound influence on the increase in their total number than is the case with the crypts. This is especially true in early childhood. The average calculated total number of glands for the ninth month fetuses was 231,341, and for the fetuses of the tenth month was 336,105. Thus the increase in the glands in this period seems to run nearly parallel with that of the crypts. The variation in the total number of glands is not so marked as one would expect. The average calculated total number at birth is about 490,000. Case 10, the largest stomach of this series, gave a total estimated count of 866,977 glands. There was no decrease in the number of glands per square millimeter in this instance. The child

TABLE 16.—*Number of Times the Total Number of Crypts and Glands Increases from Different Ages to Maturity*

Age	Average Total Number of Crypts	Number of Times Increase to Maturity	Average Total Number of Glands	Number of Times Increase to Maturity
9th fetal month	96,041	33.37	231,341	59.32
10th fetal month	138,935	23.07	336,105	40.83
Birth	204,625	15.66	489,432	28.04
2 months	691,696	4.63	1,770,634	7.76
5.5 months	858,558	3.73	2,880,478	4.77
7 months	909,108	3.52	3,062,639	4.48
17 months	1,386,781	2.31	8,232,758	1.16
22 months	1,137,220	2.81	6,572,952	2.09
2 years	1,523,587	2.10	9,003,438	1.52
3 years	1,024,773	3.12	5,937,202	2.31
6.5 years	1,693,831	1.89	10,087,085	1.36
15 years	4,077,763	—0.78	17,937,421	—0.76
Adult	3,205,508	0.00	13,724,167	0.00

TABLE 17.—*Volume (Weight), Surface Area, Total Number of Crypts and the Estimated Total Number of Glands at Various Ages Expressed in Terms of Percentage of the Adult Figure for These Factors*

	Percentage of the Adult			
Age	Volume	Total Number of Crypts	Total Number of Glands	Surface Area
9th fetal month	2.6	2.8	1.5	5.2
10th fetal month	2.0	4.0	2.2	5.8
Birth	4.6	5.9	3.1	7.3
2 months	8.7	20.2	11.9	24.9
5.5 to 7 months	16.1	24.5	20.1	29.6
17 to 36 months	21.1	35.5	50.3	34.6
6.5 years	41.8	49.4	68.2	46.6
Maturity	100.0	100.0	100.0	100.0

was stillborn so the large size of the stomach was not due to the ingestion of food.

From birth until two postnatal months there is a rapid increase in the calculated total number of glands. From birth to this time, however, the surface area of the mucosa increases about three and one-half times. Evidently, then, there must be a rapid increase in the total number of glands in the stomach during this period, concomitant with the increase in the surface area of the gastric mucosa. The total

number of glands in the stomach at 2 months is approximately 1,770,000 (Table 10). At 5½ and at 7 months the calculated number has reached approximately 3,000,000. By 2 years this has been increased to about 8,000,000, and the total number at 6½ years approximates 10,000,000. By 15 years (Case 42) the total number of glands is in the neighborhood of 18,000,000. The area of the mucosa in this specimen was quite high compared with that in the adults examined; hence the total number of glands runs proportionately higher than in maturity. The average calculated total number of glands in the stomachs of the three adults was 13,724,167.

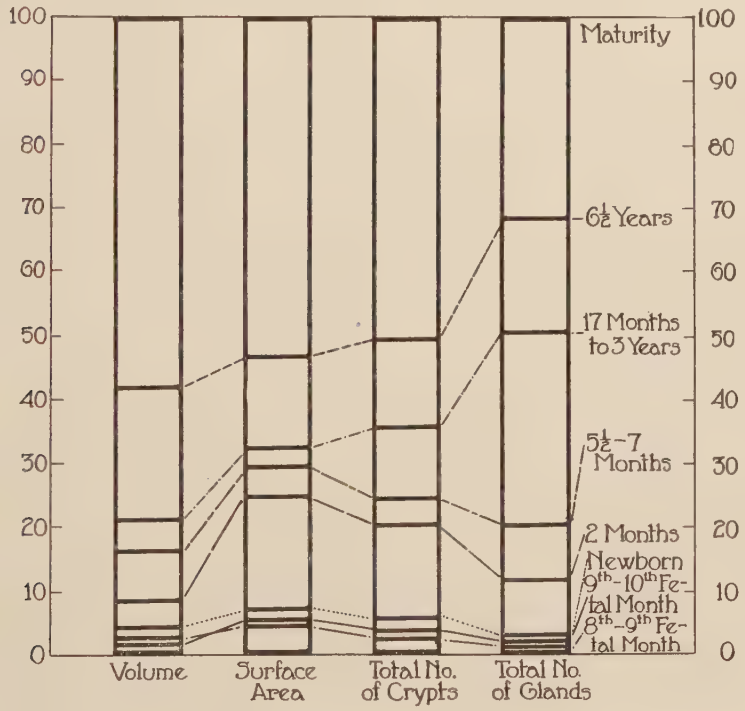

Fig. 12.—A graph showing volume (weight), surface area, total number of crypts and total number of glands at various ages, expressed as percentages of the average adult figures for these structures. Ordinates: percentages of the adult.

Table 16 shows the number of times the total number of gastric crypts and glands increase from different ages to maturity. From the ninth fetal month to maturity, the total number of crypts increases 33.37 times, while during the same period the glands increase 59.32 times. From the tenth fetal month to maturity the crypts increase twenty-three fold, and the glands forty fold. From birth to maturity the increase in crypts is about fifteen fold and the glands twenty-eight

fold. From two months to maturity the increase is markedly less, being 4.63 for the crypts and 7.76 for the glands. This decrease is more marked in respect to the number of glands than is the case of the crypts; it is due to the higher relative number of glands in early childhood.

Table 17 and Figure 12 show weight and surface area of the stomach, the total number of crypts and glands at different ages expressed in terms of percentage of the adult. The high percentages of the total number of glands from 17 months to 6½ years is due to the relatively larger number of glands per unit area at these ages as compared with the adult. This holds true in a lesser measure for the crypts.

V. SUMMARY

1. The number of gastric crypts per square millimeter of human gastric mucosa can be counted with accuracy if a proper technic is employed. There is a steady increase in the number of these structures per square millimeter in the latter part of fetal life. Following birth, there is a temporary arrest in the growth of number per unit area until the third postnatal month. After this time there is again a steady increase until 17 months. The number is constant through early childhood. Between 6½ and 15 years there is a drop of about one-eighth in the number per unit area. After this decrease there is no subsequent constant change in the number of crypts per unit area.

2. The gastric glands follow the same general course of development as the crypts. Their increase is rapid in the last two fetal months and their number per unit area remains fairly constant until 2 postnatal months. The increase is rather rapid (220 per cent.) up to 5½ to 7 months. From this period until 6½ years they remain practically constant. By 15 years there is a drop of one-third in the number per square millimeter. This value remains fairly constant thereafter, although there is some evidence of a slight decline throughout adult life.

3. The area of the gastric mucosa is a variable factor. In the four sets of data given its development follows the same type of curve. The surface area of the mucosa increases about thirteen fold between birth and maturity.

4. The total number of gastric crypts increases about sixteen fold between birth and maturity. The calculated average number in the new-born (thirteen cases) is 204,625; the calculated average number in the adult (three cases) is 3,205,508.

5. The total number of gastric glands increases twenty-eight fold between birth and maturity. The calculated average number in the

new-born (thirteen cases) is 489,432; the calculated average number in the adult (three cases) is 13,724,167.

6. The ratio of the number of glands per crypt shows a constant increase from the fetal period to middle childhood and then undergoes a decrease. From the ninth fetal month to 2 postnatal months it is about 2.5; at 5½ and at 7 postnatal months it is 3.3; from 17 months to 6 years it is nearly 6.0 and in the adolescent and the adult, approximately 4.3.

I wish to express my thanks to Dr. R. E. Scammon for his many suggestions throughout the course of this study, and for his valuable aid in the preparation of the manuscript.

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A QUANTITATIVE STUDY OF THE FETAL GROWTH CHANGES IN THE PARTS OF THE HUMAN STOMACH WALL[1]

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EIGHT FIGURES

INTRODUCTION

The importance of an accurate knowledge of the structure of the stomach during the growth period is evidenced by the numerous publications on the subject. At the present time the qualitative changes in the various layers of the stomach wall are well described, there are considerable published data available on the ponderal and capacity growth in this viscus, and the position and anatomic relations of the ventriculus, at all ages, have been considered in detail in the literature. Quantitative studies have been made of the growth changes in the gastric mucosa, and the dimensional growth of the gastric crypts and glands has been considered to a certain degree. There are numerous measurements of the thickness of the various laminae of the stomach wall scattered throughout the literature. There is, however, almost no information on the quantitative interrelationship of the various laminae of the gastric wall. It is the purpose of this paper to present data on this phase of stomach growth in the fetus and newborn infant. Computations are made of the quantities of the different tissues concerned in the architecture of the stomach wall. It is hoped that these data, and material dealing with the postnatal changes which may be added later, will be of

[1] From the Department of Anatomy, University of Minnesota. This work was done under the direction of Prof. R. E. Scammon, to whom sincere thanks are due.

some value in the interpretation of gastric physiology in the developmental period.

MATERIAL AND METHODS

The material used in this study was collected from necropsies of infants and children, which were conducted by the Department of Pathology of the University of Minnesota and by the Children's Bureau of the Department of Labor, Washington, D. C., under the direction of Dr. F. L. Adair. The material consists of forty-five fetuses and newborn infants from 5.44 fetal months to birth, calculated age. The ages were computed from the formulae of Scammon and Calkins ('23). Their distribution is as follows: sixth fetal month, two cases; seventh fetal month, two cases; eighth fetal month, four cases; ninth fetal month, four cases; tenth fetal month, ten cases; birth, twenty-three cases. The forty-five stomachs used in this study were selected from a series of more than one hundred specimens, the remainder of which were rejected as unfit for use.

The stomachs of the fetuses and newborn infants were fixed in toto, being filled with the fixing fluid and immersed in a dish containing the same fluid. This method of fixation satisfactorily eliminated all major mucosal folds and the resulting surface was, for all practical purposes, flat (fig. 1). Zenker's fluid plus acetic acid was used in all cases. The stomachs were sometimes brought from necropsy in strong formaldehyde solution; upon arrival at the laboratory, they were washed at once and placed in Zenker's solution. The tissue in all cases was fixed for twenty-four hours, washed in running water for the same length of time, and advanced by degrees to 70 per cent alcohol. The stomachs were then taken from the alcohol, drained to remove excess fluid, and weighed in a moist chamber. Pieces of the stomach wall exactly 1 cm. square were cut, with a Ballantyne's knife, from the viscus so as to transect all the constituent layers. These pieces were taken from approximately the same region in all the stomachs. This area may be described as being

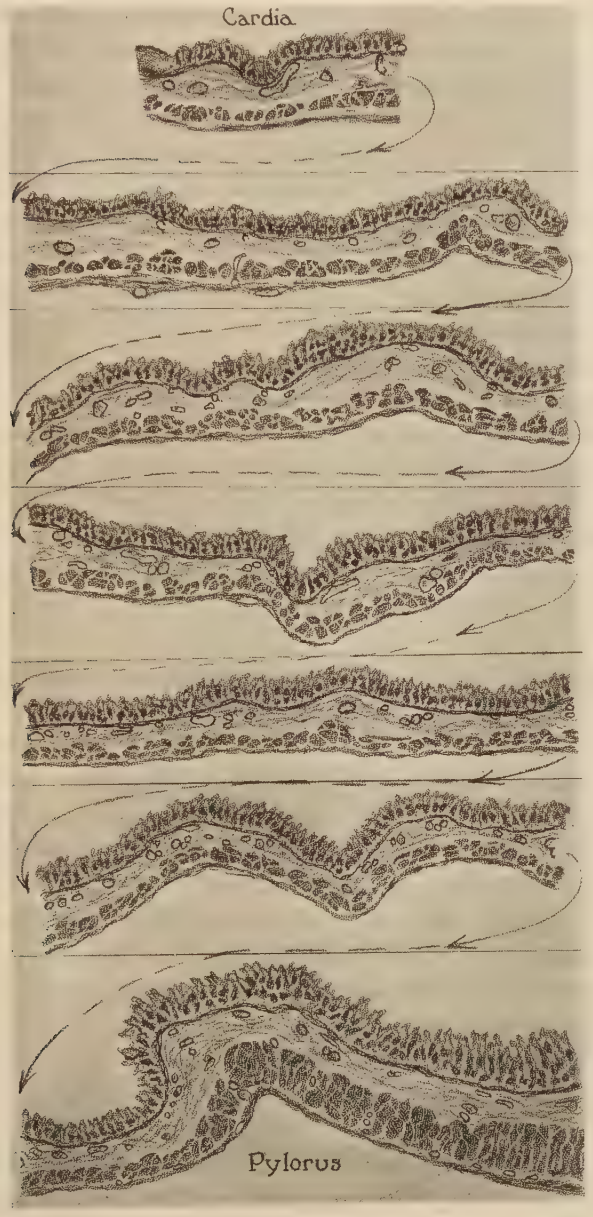


Fig. 1 A drawing, made with the aid of an Edinger projection apparatus, of a strip of the stomach wall, extending from cardia to pylorus, of a newborn infant. × 7, approximately.

about the point where the midtransverse and the midsagittal planes of the stomach transect on the ventral surface of the viscus. The pieces so cut were weighed in a moist chamber.

These portions of the stomach were dehydrated, cleared in xylol, infiltrated and embedded in paraffin, cut at 10 μ, colored in Mallory's connective-tissue stain, and mounted in Canada balsam. The dehydration, clearing, and embedding were carried on for the same length of time with all pieces of tissue. Conditions identical to those described above were maintained in so far as possible in all cases.

In a number of stomachs strips were cut also extending from cardia to pylorus. These portions were analyzed by the procedure outlined below. The results of these analyses showed that the region selected for study was typical for the major portion of the stomach wall and could be used as a basis for computations on gravimetric changes. The thickening of all layers at the pylorus was almost exactly compensated for by the thinning in the cardiac portion of the stomach (fig. 1).

Two sections, taken at different levels in each block, were projected at a magnification of 250 diameters and outlined, with a sharp pencil, upon paper of standard thickness. The different parts thus outlined were cut out with fine scissors and the paper representing these parts weighed. When each part so cut out had been weighed, the whole was summated. From this total the percentage values of the various parts of the gastric wall, as seen in cross-section, were calculated. As an example, let it be assumed that the total paper weight of the projected cross-section area of the stomach wall is 7.3641 grams, and that the paper weight of the area representing the surface epithelium is 0.2585 gram. The percentage value of the surface epithelium, thus calculated, is $(0.2585 \div 7.3641) \times 100$, or 3.51 per cent of the total cross-section area of the stomach wall. The same procedure may be carried out with the remaining parts of the gastric wall. It was necessary to fix an arbitrary standard for the separation of the morphologic parts of the epithelial elements, the

surface epithelium, crypt epithelium, and the glands. This method of division is illustrated by figure 2. The remaining parts of the stomach wall are, excepting the muscularis mucosae, sharply defined anatomically, and no difficulty was encountered in separating them.

The percentage values thus derived were used to obtain the weights of the various parts of the block of stomach tissue. The weight of the piece of tissue and the percentage values of its component parts as seen in the cross-section being known, the actual weight, in grams, of each part may be computed by taking the percentage that each part comprises of

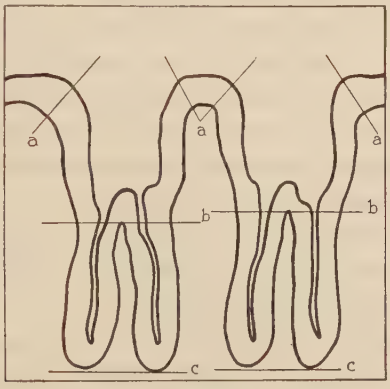


Fig. 2 Schema of the arbitrary standard of division used in the separation of the epithelial elements. Surface epithelium enclosed by lines *a*. Crypt epithelium enclosed by lines *a* and *b*. Glands enclosed by lines *b* and *c*.

the entire block. As an example, let it be assumed that the weight of 1 sq.cm. of stomach wall is 0.151 gram and that the surface epithelium, as seen in cross-section, is 3.96 per cent of the total area. The actual weight of the surface epithelium, thus calculated, is 3.96 per cent of the weight of 1 sq.cm. of stomach wall (in this case, 0.151 gram), or 0.00598 gram. The same procedure may be followed with all the parts of the stomach wall, namely, surface epithelium, crypt epithelium, glands, remainder of the mucosa, muscularis mucosae and submucosa, longitudinal and oblique muscle, circular muscle, remainder of the muscularis. By taking the weights

of the parts of 1 sq.cm. of gastric wall and multiplying them individually by the surface area of the mucosa in terms of square centimeters, the weight of each part for the entire stomach can be computed. The figures so obtained can be summated and the result checked against the observed weight of the ventriculus. If the calculated weight, derived as described above, approximates the observed weight, a check is obtained of the method of determining the percentage values of the parts and their weights and of the means of determining the surface area of the mucosa.

This method of quantitative study of the changes in the parts of the stomach makes it necessary to assume that the specific gravity of the types of tissue involved is the same. This assumption is believed to be sound, because the tissue had been fixed and partially dehydrated before the initial weighings were made. Actual tests of the specific gravity of these fixed tissues are practically impossible to make, because of the difficulties involved in isolating them. Determinations made with bits of the several tissues composing the stomach wall indicated that if a difference in specific gravity does exist, it is very slight after fixation.

The surface area of the gastric mucosa was determined by the method described by Scott ('25). The stomach was divided into halves by incisions along the greater and lesser curvatures, and a plaster cast made of the mucosal surface. Thin tissue paper was then placed on the cast, moistened with water, molded carefully over the surface irregularities, and allowed to dry. The tissue paper was then removed from the cast, flattened, and the outlines traced on standard-thickness paper, which was cut out and weighed. Having the total weight of the paper and its known weight per square centimeter, the area was easily calculated.

TREATMENT OF DATA

The data obtained in this study were not particularly adaptable to graphic or numerical treatment. The graphic analysis of data is limited to simple histograms. Means were taken

of the percentage values and their variability measured by two methods, that of mean deviation and that of relative mean deviation. These two measures of variability expressed as formulae are:

Mean deviation:

$$MD = \frac{\Sigma d}{n}$$

Σd = sum of the deviants from the arithmetic mean
n = number of cases

Relative mean deviation:

$$RMD = \frac{M}{\frac{(\Sigma d)}{n}} \times 100$$

M = arithmetic mean
Σd = sum of the deviants from the arithmetic mean
n = number of cases

This formula may be simplified to read:

$$RMD = \frac{M}{MD} \times 100$$

M = arithmetic mean
MD = mean deviation

LITERATURE

There are many observations and measurements of the various tunics of the gastric wall scattered through the literature. With few exceptions, the investigators making these observations were primarily interested in some particular phase of the field and have recorded few coordinated sets of data that may be used for comparison in this study. The dimensions of the various parts of the mucosa have been taken most frequently. The dimensional changes that occur in the crypts and glands during fetal development in the human species have been recorded by Toldt ('80), Baginsky ('82), Kollmann ('98), and Johnson ('10). The last-named author considered the epithelial growth to take place by the enlargement of the crypts as well as by the formation of new ones. He found the glands to vary considerably in length and breadth.

Baginsky ('82), in his study of the fetal and postnatal human stomach, made numerous measurements on the thickness of the layers of the stomach wall in its several regions. He gave no record of the number of measurements made or whether the figures given were averages of several readings. This author believed that there was a growth in the length and an increase in the number of glands, but that their relative mass decreased. He also stated that there was an increase in the thickness of the muscularis mucosae, although after an examination of the figures recorded this appears to be erroneous. There was a constant increase, with age, in the thickness of the circular and longitudinal muscle layers. Baginsky pointed out that there was a precocious development in the muscle layers of the stomach immediately before birth and shortly thereafter. The submucosa lost its cellular character more and more with age, and there was a decrease in lymphoid tissue and in the size of the lymph vessels between the muscle layers of this viscus.

In making a study of congenital pyloric stenosis, Gran ('96) has recorded measurements on thickness of the various layers of the normal ventriculus in an infant of four months.

The thickness of the tunics of the stomach wall in the human adult has been measured by a number of observers. There is a wide variance in the results given, although the measurements were taken, presumably, at the same region of the stomach. The thickness of the mucosa at the cardia, according to Piersol ('16), is 0.35 to 0.55 mm., and, according to Testut ('12), 1 mm., while Kupffer ('83) gives it as 0.7 mm. Kupffer ('83) has recorded the thickness of the mucosa at the pylorus as 1 mm., while Piersol ('16) and Testut ('12) are in close agreement with their measurements of 1.5 to 2 mm. (Piersol) and 2 mm. (Testut). Korolenko ('02) gives the thickness of the mucosa as 0.36 mm., but does not state in what region of the stomach the observation was made. The mensurations of Jonnesco ('01) show a marked thickening of the submucosa in the pyloric region. The thickness of the muscularis is subject to considerable variation—a fact

shown by the measurements of Kölliker ('67), Testut ('12), and Jonnesco ('01). Stöhr ('05) found the thickness of the stomach wall to be from 2 to 3 mm., while Jonnesco ('01) records it as 3 mm. Bruch ('49) found the total thickness of the gastric wall to be from 3.2 to 4.2 mm. at the pylorus and 2.1 mm. in the middle zone. He gives the thickness of the muscularis as 1.05 mm. and the mucosa and submucosa as 1.05 mm. in the middle zone of the stomach. Frerichs ('46) made measurements of the length and breadth of the gastric glands in the young and adult human, the cat, and in the newborn pig. He found the fundic glands in the adult human to be 1.05 mm. in length and 0.04 to 0.05 mm. in breadth, while in children aged nine months to two years the dimensions are 0.52 mm. and 0.021 to 0.027 mm., respectively. In the young cat the length of the glands is 0.211 to 0.263 mm.; in the adult cat, 0.52 to 0.702 mm., and in the newborn pig, 0.350 mm. Frerichs believed that the fundic glands of the stomach were smaller in all dimensions in the young than in older individuals. Frey ('75) stated that in children the gland tubules are smaller in caliber and shorter than in the adult.

It seems from an examination of these data that the various authors are in agreement that there is a thickening of all layers of the stomach wall at the pylorus, that there is a thinning of all layers of the stomach wall at the fundus, and that the middle zone represents an approximate mean of the two.

Mall ('96), in a study of the vessels and walls of the dog's stomach, has recorded measurements at various intervals on a strip of stomach wall, taken from the ventral surface of the viscus, extending from cardia to pylorus. Each mensuration given is an average of from ten to twenty observations. From Mall's observations it may be seen that the thickness of the middle zone of the dog's stomach represents almost an exact mean of the cardia and of the pylorus. This, however, does not hold for all the constituent layers of the stomach wall.

SUMMARY OF FINDINGS AND COMMENT

1. The growth changes of the surface epithelium

The surface epithelium of the stomach may be defined as that part of the mucous membrane which is in direct contact with the cavity of this viscus. During later fetal life and at birth it is usually covered with a thick layer of mucus. It may be marked off sharply from the epithelium which extends downward into the crypts, by virtue of its position more than by its staining reactions. In fetuses of the latter half of intra-uterine life, the cells which form this layer are typical high columnar epithelial cells with basally located nuclei. The cells are smaller at the base than at the surface, and the group between two crypts has a fan-shaped appearance. This is especially marked in the stomach of the newborn infant. Mucous cells are rarely seen in the surface epithelium, although they are plentiful in the crypts (Toldt, '80; Disse, '05).

The surface epithelium in a fetus of the sixth month comprises 3.12 per cent of the cross-section area of the stomach wall. The changes in this relation which occur with an increase in fetal age are not great. Between the ages of six and ten fetal months this value fluctuates between 3 and 4 per cent (table 1). At the tenth fetal month the relative amount of surface epithelium has increased to 4.38 per cent. However, the variability has increased also, and this rise is not marked enough to warrant a definite statement that the amount of epithelium has undergone great change. The mean deviation of the observations on ten different individuals is 0.77 per cent and the relative mean deviation is 17.58 per cent (table 1). At birth the average percentage of surface epithelium has dropped to 3.32, with a mean deviation of 1.34 per cent and a relative mean deviation of 40.24 per cent. It is probable that this change is statistically significant. The relative amount of surface epithelium, as seen in a cross-section area of the stomach wall, can therefore be said to be practically constant throughout the later months of fetal life, although it appears slightly greater at the tenth fetal month than in the newborn.

If the mucosa be regarded as 100 per cent in order to eliminate from our figures the influence of changes in the submucosa and muscularis, one obtains a clearer conception of the changes in the surface epithelium. When this procedure is carried out, the surface epithelium is considered as the relative amount seen in a cross-section area of the mucous membrane. In the sixth fetal month the surface epithelium, computed by this means, forms 15.74 per cent of the mucous membrane. This figure is practically unchanged until the

TABLE 1

The mean percentage values of the various parts of the stomach from the sixth fetal month to birth

NUMBER OF CASES	CALCULATED AGE IN FETAL MONTHS	SURFACE EPITHELIUM	CRYPT EPITHELIUM	GLANDS	REMAINDER OF MUCOSA	MUSCULARIS MUCOSAE AND SUBMUCOSA	LONGITUDINAL AND OBLIQUE MUSCLE	CIRCULAR MUSCLE	REMAINDER OF MUSCULARIS
2	5.60	3.12	2.61	4.54	9.50	13.75	2.99	21.49	41.90
2	6.51	3.74	3.07	6.13	11.47	15.75	3.05	28.47	28.30
4	7.50	3.43	5.47	10.73	15.78	14.56	2.80	23.55	23.84
4	8.39	3.76	7.83	17.52	21.88	12.64	2.66	12.66	21.02
10	9.37	4.38	7.19	14.19	14.26	9.45	9.26	18.45	22.84
Mean deviation		0.77	0.73	0.25	0.37	0.40	0.55	0.93	1.23
Relative mean deviation		17.58	10.15	1.76	2.59	4.23	5.94	5.04	5.38
23	10.37	3.32	4.26	8.99	14.02	30.50	6.01	13.83	19.02
Mean deviation		1.34	1.44	1.19	0.79	4.36	1.02	2.55	1.44
Relative mean deviation		40.24	33.90	13.22	5.68	14.30	16.99	18.46	7.56

eighth fetal month, when it drops to 9.71 per cent. This occurs at about the inception of the period of rapid increase in the number of crypts per square millimeter of gastric mucosa (Scott, '25). There is a further drop in this ratio in the ninth fetal month, for at this time the surface epithelium forms 7.39 per cent of the mucosa. At the tenth month of intra-uterine life and at birth this value is between 10 and 11 per cent (table 2). The variability has increased, however, the mean deviation being 1.72 per cent and the relative mean deviation, 15.80 per cent, and 3.21 and 31.04 per cent, respectively.

It is possible, by disregarding the connective tissue, blood vessels, and lymphoid tissue, to attack the problem in another manner. Connective tissue, blood vessels, and lymphoid tissue are evidently more subject to change in volume than are the other types of tissue involved in the architecture of the stomach wall. In figuring the percentage values of the parts, if the paper weights representing the above-mentioned elements are omitted from the summation of the total paper weight, the surface epithelium, crypt epithelium, glands, and the layers of the muscularis can be calculated as 100 per cent.

TABLE 2

The mucosa calculated as 100 per cent, with the mean percentage values of its component parts from the sixth fetal month to birth

NUMBER OF CASES	CALCULATED AGE IN FETAL MONTHS	SURFACE EPITHELIUM	CRYPT EPITHELIUM	GLANDS	REMAINDER OF MUCOSA
2	5.60	15.74	13.42	22.96	47.92
2	6.51	15.30	12.61	25.16	46.92
4	7.50	9.71	15.51	30.09	44.68
4	8.39	7.39	15.37	34.35	42.90
10	9.37	10.90	17.93	35.47	35.69
Mean deviation		1.72	1.48	1.36	1.35
Relative mean deviation		15.80	8.24	3.84	3.77
23	10.37	10.35	13.45	29.33	46.86
Mean deviation		3.21	2.99	1.10	6.08
Relative mean deviation		31.04	22.22	3.75	12.97

This procedure gives a percentage for the surface epithelium which does not change materially during the fetal months represented in the series studied. The percentage of surface epithelium, as determined by this treatment, fluctuates from 7.51 to 8.97, the highest value being in the sixth fetal month and the lowest in the eighth prenatal month. These figures, together with measures of their variability, are given in table 3.

The calculated weight of the surface epithelium, in 1 sq.cm. of gastric wall and in the entire stomach, may be derived by the means described in the section on material and methods. The computed weight of the surface epithelium for 1 sq.cm.

of gastric wall in the sixth prenatal month is 0.003 gram; in the seventh fetal month, 0.005 gram; in the eighth fetal month, practically the same as the preceding month, and in the ninth prenatal month, 0.005 gram (table 4). In the tenth month of intra-uterine life this calculated weight has increased to 0.007 gram and at birth is 0.006 gram. The variability in the neonatal series is relatively large, the mean deviation being 0.003 gram and the relative mean deviation, 47.17 per cent (table 4).

TABLE 3

The epithelial and muscle elements calculated as 100 per cent, with the mean percentages of their component parts from the sixth fetal month to birth

NUMBER OF CASES	CALCULATED AGE IN FETAL MONTHS	SURFACE EPITHELIUM	CRYPT EPITHELIUM	GLANDS	LONGITUDINAL AND OBLIQUE MUSCLE	CIRCULAR MUSCLE
2	5.60	8.97	7.64	13.05	8.60	61.73
2	6.51	8.39	6.90	13.78	6.89	64.02
4	7.50	7.51	11.90	23.20	6.13	51.25
4	8.39	8.45	17.63	39.43	5.97	28.50
10	9.37	8.17	13.42	26.52	17.32	34.57
Mean deviation		1.38	1.11	0.90	0.75	2.07
Relative mean deviation		16.89	8.27	3.39	4.35	5.99
23	10.37	8.75	11.29	24.81	16.58	38.57
Mean deviation		2.85	2.35	2.04	1.64	5.74
Relative mean deviation		32.57	20.86	8.22	9.89	14.88

The amount, in weight, of surface epithelium in the entire stomach may be calculated by multiplying the amount, in weight, of surface epithelium in 1 sq.cm. by the surface area of the gastric mucosa expressed in terms of the same unit. This calculated weight of surface epithelium is 0.032 gram in the sixth prenatal month, 0.084 gram in the seventh fetal month, and has increased to 0.138 gram by the ninth month of intra-uterine life (table 5). In the tenth fetal month and at birth the computed weights of the surface epithelium are 0.238 and 0.214 gram, respectively. The variability in the last prenatal month is considerable, the mean deviation being 0.054 gram and the relative mean deviation, 22.49 per cent. These figures, together with measures of their variability, are given in table 5.

TABLE 4

The mean computed weights, in grams, of the various parts of 1 sq.cm. of stomach wall from the sixth fetal month to birth, calculated from the percentage values, the averages of which are shown in table 1, and from weights, the averages of which are shown in table 9

NUMBER OF CASES	CALCULATED AGE IN FETAL MONTHS	SURFACE EPITHELIUM	CRYPT EPITHELIUM	GLANDS	REMAINDER OF MUCOSA	MUSCULARIS MUCOSAE AND SUBMUCOSA	LONGITUDINAL AND OBLIQUE MUSCLE	CIRCULAR MUSCLE	REMAINDER OF MUSCULARIS
2	5.60	0.003	0.003	0.005	0.010	0.015	0.003	0.023	0.045
2	6.51	0.005	0.004	0.008	0.014	0.019	0.004	0.035	0.034
4	7.50	0.005	0.007	0.014	0.021	0.020	0.004	0.032	0.032
4	8.39	0.005	0.011	0.023	0.029	0.017	0.004	0.017	0.023
10	9.37	0.007	0.011	0.021	0.021	0.014	0.014	0.028	0.034
Mean deviation		0.002	0.002	0.004	0.003	0.002	0.002	0.005	0.006
Relative mean deviation		24.39	17.23	17.13	14.54	16.20	16.09	17.03	17.18
23	10.37	0.006	0.007	0.015	0.023	0.050	0.010	0.023	0.031
Mean deviation		0.003	0.003	0.003	0.003	0.009	0.002	0.004	0.003
Relative mean deviation		47.17	39.15	18.98	12.11	18.17	21.75	17.84	8.50

TABLE 5

The mean weights, in grams, of the various parts of the stomach from the sixth fetal month to birth, as calculated from weights, the averages of which are shown in table 4, and from surface areas, the averages of which are shown in table 9

NUMBER OF CASES	CALCULATED AGE IN FETAL MONTHS	SURFACE EPITHELIUM	CRYPT EPITHELIUM	GLANDS	REMAINDER OF MUCOSA	MUSCULARIS MUCOSAE AND SUBMUCOSA	LONGITUDINAL AND OBLIQUE MUSCLE	CIRCULAR MUSCLE	REMAINDER OF MUSCULARIS
2	5.60	0.032	0.027	0.047	0.098	0.141	0.031	0.221	0.430
2	6.51	0.084	0.069	0.137	0.259	0.351	0.067	0.635	0.609
4	7.50	0.110	0.177	0.350	0.509	0.467	0.090	0.761	0.760
4	8.39	0.138	0.286	0.633	0.791	0.459	0.098	0.458	0.761
10	9.37	0.238	0.389	0.779	0.781	0.519	0.506	1.010	1.254
Mean deviation		0.054	0.061	0.158	0.152	0.108	0.097	0.193	0.255
Relative mean deviation		22.49	15.62	20.27	19.39	20.75	19.15	19.14	20.37
23	10.37	0.214	0.271	0.577	0.910	1.964	0.387	0.906	1.238
Mean deviation		0.099	0.094	0.117	0.157	0.423	0.097	0.243	0.245
Relative mean deviation		46.21	34.85	20.25	17.27	21.52	25.04	26.82	19.82

2. Growth changes of the crypt epithelium

The gastric crypts (foveolae gastricae) are small pit-like depressions in the mucosa, having at birth an average depth of 0.11 mm. and an average breadth of 0.02 to 0.05 mm. (Johnson, '10). The ostia of the gastric glands (glandulae gastricae propriae) may be seen at their basal ends. The shape of the mouth of the crypt varies; some may be round, some oval, and others appear to be elongated slits in the surface epithelium. Their number per square millimeter of gastric mucosa has been determined in the last two months of intra-uterine life and at birth (Toldt, '80, and Scott, '25).

In the latter part of fetal life and at birth the epithelial cells lining the crypts may have slender basal prolongations (Baginsky, '82, and Fischl, '91). These cells are mucoid in character and are actively secreting before birth (Lewis, '12). The gastric crypts at the sixth fetal month are deeper and broader than those seen in the later fetuses and at birth. They receive the ostia of one or more gastric glands at this stage of development.

The crypt epithelium forms 2.61 per cent of the cross-section area of the gastric wall in the sixth fetal month. This value has increased to 3.07 per cent by the middle of the seventh prenatal month and is 5.47 per cent by the middle of the eighth month of intra-uterine life. In the ninth and tenth fetal months it is 7.83 and 7.19 per cent, respectively. The variation in the middle of the tenth fetal month is not great, the mean deviation being 0.73 per cent and the relative mean deviation, 10.15 per cent (table 1). By the time of birth the relative amount of crypt epithelium, as seen in cross-section area of the stomach wall, is 4.26 per cent. The variability has increased, however, the mean deviation being 1.44 per cent and the relative mean deviation, 33.90 per cent (table 1). This decrease in the percentage of crypt epithelium at birth is influenced by other factors, particularly by the marked increase in the connective-tissue elements at birth.

If the mucosa be regarded as 100 per cent, the influence of changes which occur in the submucosa and muscularis is

removed and a clearer conception is obtained of the changes in the crypt epithelium. When considered in this manner, the crypt epithelium in the sixth fetal month forms 13.42 per cent of the gastric mucosa as seen in the cross-section area. In the seventh fetal month the crypt epithelium, so calculated, is 12.61 per cent and in the eighth and ninth fetal months, 15.51 and 15.37 per cent, respectively, of the mucosa. By the tenth fetal month this value has increased to 17.93 per cent, with a mean deviation of 1.48 per cent and a relative mean deviation of 8.24 per cent (table 2). By the time of birth the relative value of the crypt epithelium has dropped to 13.45 per cent, with a mean deviation of 2.99 per cent and a relative mean deviation of 22.22 (table 1). It is apparent from these figures that there is some actual decrease in relative amount of crypt epithelium at birth. This may be due to changes in the remainder of the mucosa, exclusive of the surface epithelium and glands, or it may be due to the actual shortening and decrease in breadth of the crypts which have occurred by this time.

It is possible, by disregarding the obviously more variable elements of the stomach wall, such as connective tissues, blood vessels, and lymphoid tissue, to attack the problem from a different angle. The surface epithelium, crypt epithelium, glands, and the layers of the muscularis may be calculated as 100 per cent, as described in the paragraphs on surface epithelium. The data which form the basis of the following paragraphs are found in table 3.

When the parts of the epithelial layer and the muscle layer of the stomach are calculated as 100 per cent, the crypt epithelium in the sixth fetal month forms 7.64 per cent of the total. In the next prenatal month this value is 6.90 per cent and by the middle of the eighth fetal month it has increased to 11.90 per cent. The values from which this average is computed range from 9.26 to 14.41 per cent, indicating a relatively wide variation. In the ninth and tenth months of intra-uterine life the crypt epithelium, so calculated, averages 17.63 and 13.42 per cent, respectively. The mean devia-

tion is 1.11 per cent and the relative mean deviation, 8.27 per cent, in the tenth prenatal month. At birth this value is still lower, the crypt epithelium being 11.29 per cent, with a mean deviation of 2.35 per cent and a relative mean deviation of 20.86 per cent. This large variation makes it seem improbable that there is as much of a decrease in the crypt epithelium as the average would indicate.

By taking the weight of 1 sq.cm. of gastric wall and the percentage of crypt epithelium as seen in the cross-section area of the stomach wall, it is possible to calculate the weight of the crypt epithelium for this portion of the ventriculus. This procedure has been described in detail in the section on material and methods.

The weight of the crypt epithelium, calculated in the manner described above, for the sixth prenatal month is 0.003 gram. There is a steady increase in this weight with the advance in fetal age, the value at the ninth fetal month being 0.011 gram (table 4). By the first third of the tenth fetal month the computed weight of crypt epithelium averages 0.011 gram per square centimeter. The mean deviation for this series is 0.002 gram and the relative mean deviation, 17.23 per cent (table 4). At birth there is an apparent drop in the calculated weight of crypt epithelium per square centimeter of stomach wall, the value being 0.007 gram, with a mean deviation of 0.003 gram and a relative mean deviation of 39.15 per cent. The crypts by this time have become much shorter and the lumen is narrower than that seen in earlier stages of development. The influence of the variability of the material is more evident than in the younger fetuses studied.

If the weight of the crypt epithelium per square centimeter of stomach wall is multiplied by the surface area of the gastric mucosa, an estimate may be derived of its weight in the entire stomach.

The total crypt epithelium in the stomach of a fetus of the sixth month, by calculation, weighs 0.027 gram; in the seventh fetal month, 0.069 gram, and 0.177 gram in the eighth month

of prenatal life. By the ninth month of intra-uterine life this value has increased more than 0.1 gram and at the tenth fetal month it is 0.389 gram (table 5). The mean deviation for the average at this age is 0.061 gram and the relative mean deviation, 15.62 per cent. At birth the computed weight of crypt epithelium has decreased to 0.271 gram, with a mean deviation of 0.094 gram and a relative mean deviation of 34.85 per cent. There is then, apparently, an actual decrease in the weight of the crypt epithelium as determined by the methods used in this study.

3. The growth changes of the gastric glands (glandulae gastricae propriae)

The development of the gastric glands has been a subject of some dispute among embryologists. That they arise from the epithelium of the stomach seems to be now beyond question (Kölliker, '79; Toldt, '80; Johnson, '10, and others). In older embryos and in the fetus the glands grow more rapidly than the crypts and become elongated and branch freely (Johnson, '10). In a 240-mm. embryo the glands occupy the basal third of the mucosa and at birth they form nearly one-half of this layer (Lewis, '12).

The increase in the number of glands has been described by Toldt ('80) and Scott ('25). Fischl ('91) described the condition of the gastric glands at birth. He found them to be broader and shorter and more widely separated than in the adult. Frey ('75) believed the glands to be smaller in all dimensions in the young than in the adult. Johnson ('10) stated that the histologic structure of the glands at birth is similar to that in the adult. Gundobin ('12), quoting Lissenko, says that the glands do not acquire the adult histologic structure until some time after the first year.

Toldt ('80) found parietal cells at the ends of the glands in the fourth and fifth months. At the sixth fetal month he described them as appearing everywhere along the sides of the glands. Kaleopothakès ('94) reported acid cells in a fetus of six months. Sewall ('79) stated that in sheep

embryos the parietal cells first appeared at the blind end of the gland. Kirk ('10), in his study of the histogenesis of the gastric glands in the pig, found parietal cells in the gastric epithelium at very early stages.

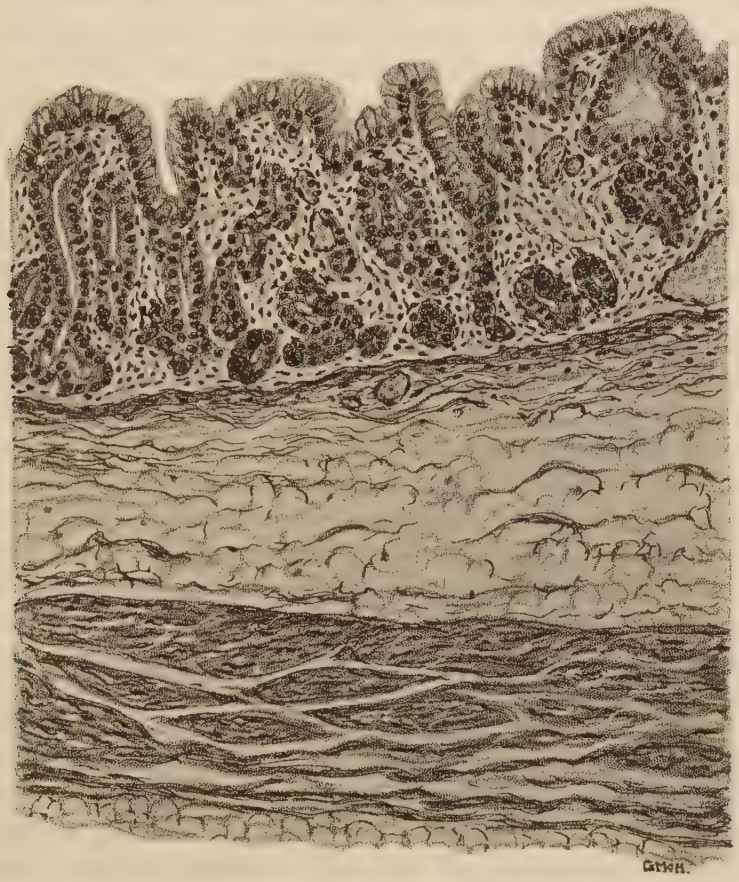


Fig. 3 A drawing of a section through the corpus gastricae of a newborn infant. × 60, approximately.

In the material studied in the present series, parietal cells were found in all stomachs that were examined. They appear to be confined to the blind end of the gland in early stages and at birth. It is possible to find an occasional cell or group of two or three cells along the side of a gland. Figure 3 is a

drawing of a section through the corpus gastricae of a newborn infant.

The gastric glands in a fetus of six months constitute 4.54 per cent of the total cross-section area of the wall of the ventriculus. By the middle of the seventh fetal month this value has increased to 6.13 per cent, and by the middle of the eighth fetal month the average is 10.73 per cent. In the first third of the ninth lunar month the percentage value of the glands averages 17.52 per cent (table 1). For the tenth prenatal month the average percentage is 14.19, with a mean deviation of 0.25 per cent and a relative mean deviation of 1.76 per cent. At birth the percentage value of the glands is still lower, being nearly 9, with a mean deviation of 1.19 per cent and a relative mean deviation of 13.22 per cent (table 1). The drop in relative amount of gland tissue, which is evident from these figures, makes its weight felt in all computations made on gland volume in this study.

When the gastric mucosa is calculated as 100 per cent, as previously described, the glands in the cross-section area of the mucosa of a sixth-month fetus comprise nearly 23 per cent of the total. In the seventh fetal month they have increased to 25 per cent; in the eighth and ninth, to 30 and 34.4 per cent, respectively. In the fetuses of the tenth month this value is practically unchanged, being 35.5 per cent, with a mean deviation of 1.36 per cent and a relative mean deviation of 3.84 per cent (table 2). At birth there is a slight reduction in the quantitative relation of glands to gastric mucosa, for at this time they form nearly 30 per cent of the total. The variability has not increased materially, the mean deviation for this series being 1.1 per cent and the relative mean deviation, 3.75 per cent.

When the epithelial and muscle elements are computed as 100 per cent, the connective tissues being disregarded, the glands comprise 13.05 per cent of the total in the sixth fetal month. In the seventh month of intra-uterine life this percentage is unchanged, but by the middle of the eighth lunar month it has increased to 23.20. In the ninth fetal month the

percentage of glands, so calculated, is at its highest point, being 39.43 (table 3). This high point in gland relation is followed by a decrease of about three-eighths of the former value. The lowest figure is reached at birth, when the glands, so computed, are 24.81 per cent of the epithelial and muscle elements. At nine fetal months the circular muscle is relatively lower in value than at any other time. This factor, no doubt, has a direct bearing upon the percentage of gland tissue present at this time.

The computed weight of the gastric glands per square centimeter in a fetus of the sixth month is 0.005 gram. The weight of the glands increases steadily up to the close of the ninth prenatal month, when it is calculated to be 0.023 gram; in the tenth month of intra-uterine life this value is 0.021 gram, with a mean deviation of 0.004 gram and a relative mean deviation of 17.13 per cent (table 4). There is a still greater decrease in gland weight per square centimeter of mucosa at birth, for at this time it is only 0.015 gram. There has been an increase in the variability of the material, however, and the mean deviation is 0.003 gram and the relative mean deviation is nearly 19 per cent (table 4).

The total weight of the gland substance may be calculated from the above figures with the aid of data on the area of the gastric mucous membrane in square centimeters. The gastric mucosa of a fetus of the sixth month is calculated to contain 0.047 gram of gland substance. The computed weight in the seventh fetal month is 0.137 gram; in the eighth prenatal month, 0.350 gram, and has increased to 0.633 gram by the first third of the subsequent month (table 5). The average calculated gland weight for the tenth-month fetuses is 0.779 gram, with a mean deviation of 0.158 gram and a relative mean deviation of 20.27 per cent. At birth the gastric mucosa is calculated to contain a little more than 0.5 gram (about one-twelfth of the total stomach weight) of gland substance. The variability measures are very close to those of the tenth fetal month (table 5).

4. Growth changes of the remainder of the mucosa

The muscularis mucosae is not included with this portion of the stomach wall, for it seemed advisable to place it with the submucosa because of its ill-defined borders in later fetal life and in the newborn infant. The remainder of the mucosa, then, is taken to be that tissue which is found above the muscularis mucosae, between and at the base of the crypts and glands. No attempt has been made to separate its components, which are areolar tissue, lymphoid tissue, blood and lymph vessels, and a few nerves. This aggregation of tissues shows more variability than the more highly differentiated parts of the stomach wall, namely, the epithelial and muscle elements.

The remainder of the mucosa in a fetus of the sixth month comprises 9.5 per cent of the total cross-section area of the gastric wall. This percentage value increases to 11.47 in the subsequent month, 15.78 in the eighth prenatal month, and is as high as 21.88 at the close of the ninth fetal month (table 1). For the tenth month of intra-uterine life the average per cent is 14.26, with a mean deviation of 0.37 per cent and a relative mean deviation of 2.59 per cent. At birth this value is not materially changed, being 14.02 per cent of the cross-section area of the stomach wall. The variability of the material has increased, however, and the mean deviation at birth is 0.79 per cent, with a relative mean deviation of 5.68 per cent (table 1).

When the mucosa is calculated as 100 per cent, it will be seen that the remainder of the mucosa, that is, the non-epithelial parts, constitutes about one-half of the mucosa at all ages except that of the tenth fetal month. In the fetuses of the tenth month the remainder of the mucosa drops to 35.69 per cent, but at birth this value has increased to 46.86 per cent. In the material earlier than ten months included in the present series, the percentage value of the remainder of the mucosa fluctuates between 47.92 and 42.90, with no indication of any steady change with age. It is interesting to

note the almost quantitative relationship which exists between the glands and the remainder of the mucosa. When one value rises, the other falls, and when the changes in percentage values are reversed, the same result follows. Table 1 shows the above changes in percentage of the remainder of the mucosa more in detail.

The computed weight of the remainder of the mucosa for 1 sq.cm. of stomach wall in a fetus of the sixth month is 0.010 gram. By the next fetal month this weight is slightly higher than in the preceding month, and by the eighth prenatal month it is 0.021 gram. The highest calculated weight recorded for the series is the average of the specimens taken in the ninth month of intra-uterine life, when the remainder of the mucosa is computed to weigh 0.029 gram (table 4). There is a slight decrease in this weight, so computed, in the tenth fetal month, when it is 0.021 gram, with a mean deviation of 0.003 gram and a relative mean deviation of 14.54 per cent. In the newborn infant this aggregation of tissues, by calculation, weighs 0.023 gram—a slight increase over the preceding month. The variability measures are interesting, for they show less variation at this time than the same measurements taken on other parts of the stomach at birth. The mean deviation is 0.003 gram and the relative mean deviation, 12.11 per cent (table 4).

The total weight of the remainder of the mucosa in the stomach of a fetus of the sixth month is 0.098 gram, as calculated by the method previously described. This value rises rapidly up to the ninth prenatal month, when it is 0.791 gram. There is a very slight decrease in the tenth lunar month, at which time the computed weight is 0.781 gram, with a mean deviation of 0.152 and a relative mean deviation of 19.39 per cent. By birth the total calculated weight of the remainder of the mucosa has increased to 0.910 gram, with a mean deviation of 0.157 gram and a relative mean deviation of 17.27 per cent. The apparent decrement in the computed weight of this part of the stomach wall in the tenth fetal month seems to be entirely within the range of normal variability

and is therefore without significance. The figures which form the basis of the above paragraph are found in detail in table 5.

5. Summary of the growth changes of the gastric mucosa

A summary of the growth changes of the mucosa is presented graphically in figures 4, 5, and 6. Figure 4 is a histogram plotted with the percentage values of the different parts of the stomach wall in their exact quantitative relations as seen in the cross-section area. This figure shows the absence of any great change in the surface epithelium. The crypt epithelium is shown to increase and then decrease—not enough, however, to return to its former value. The glands undergo the same sort of change as do the crypts. The remainder of the mucosa is also shown to increase in relative amount and, after the ninth fetal month, to undergo a regression.

Figure 5 is a histogram plotted in the same manner as figure 4. This figure represents the quantitative relations of the epithelial and muscle elements when computed as 100 per cent. Here the relationship of muscle to the gland tissue in the ninth fetal month is shown particularly well. When the glands form the most part of the mucosa, the muscle elements are at their lowest percentage values.

Figure 6 is a histogram which shows the quantitative relations of the parts of the mucous membrane when calculated as 100 per cent. This figure illustrates the quantitative relationship which exists between the surface and the crypt epithelium and that which exists between the glands and the remainder of the mucosa.

6. Growth changes of the muscularis mucosae and submucosa

The muscularis mucosae is included with the submucosa in all computations of the quantitative relations of this lamina. The muscularis is so poorly defined at birth and in the earlier fetuses studied that it was deemed advisable not

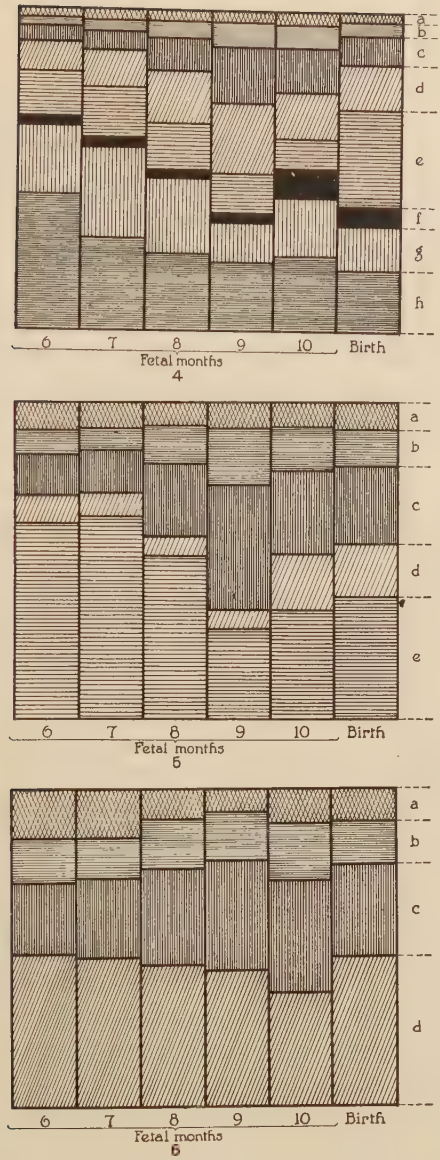


Fig. 4 The percentages of the parts of the stomach wall plotted as a histogram. *a*, surface epithelium; *b*, crypt epithelium; *c*, glands; *d*, remainder of the mucosa; *e*, muscularis mucosae and submucosa; *f*, longitudinal and oblique muscle laminae; *g*, circular muscle; *h*, remainder of the muscularis.

Fig. 5 The percentage values of the surface epithelium, crypt epithelium, glands, and the two muscle layers calculated as 100 per cent, plotted as a histogram from the data in table 3. *a*, surface epithelium; *b*, crypt epithelium; *c*, glands; *d*, longitudinal and oblique muscle; *e*, circular muscle.

Fig. 6 The mucosa calculated as 100 per cent with the mean values of its component parts plotted as a histogram from the data in table 2. *a*, surface epithelium; *b*, crypt epithelium; *c*, glands; *d*, remainder of mucosa.

to attempt to calculate this lamina separately. Welch ('23) stated that the muscularis mucosae, though incomplete, could be identified in embryos of 65 mm. (crown-rump length) and in all succeeding ages. In the present series no difficulty was encountered in identifying this muscle layer. Baginsky ('82) found the submucosa to be very cellular in early fetuses and stated that its cellular character was lost as age progressed. The observations made upon the material at hand are in agreement with this statement.

In the following discussion the term submucosa shall be considered as including the muscularis mucosae. In the fetuses of the sixth month the submucosa forms 13.75 per cent of the cross-section area of the gastric wall. By the seventh fetal month this value has increased to 15.75 per cent, and in the eighth prenatal month there is a slight decrease in the percentage value. In the ninth fetal month the submucosa represents 12.64 per cent of the total area of the gastric wall as seen in cross-section (table 1). In the average for the tenth fetal month there is evidence of a greater decrease in the relative amount of submucosa, the value at this age being 9.45 per cent. The variability is such that this decrement can be considered actual rather than apparent. The mean deviation of the series at this age is 0.40 per cent and the relative mean deviation, 4.23 per cent. At the time of birth there is a tremendous increase in the relative value of the submucosa, the percentage at this age being 30.50. The variability is greater than in the preceding ages studied, but still not marked enough to account for this great increase in percentage value. In the series of newborn infants the mean deviation is 4.36 per cent and the relative mean deviation, 14.30 per cent. The range of these observations is from 15.76 to 38.27 per cent (table 1).

The submucosa and muscularis may be calculated as 100 per cent in the same manner as the mucosa. This procedure gives a clearer conception of changes that occur in this main subdivision of the stomach wall. The submucosa, so computed, forms 17.16 per cent of the cross-section area of the

submucous and muscle coats of the stomach in the fetuses of the sixth month. This percentage value rises very steadily and by the ninth fetal month is 25.80. In the tenth lunar month this value has fallen to 15.77 per cent, with a mean deviation of 0.90 per cent and a relative mean deviation of 5.71 per cent (table 6). At the time of birth the submucosa has become relatively enormous in its proportions, as compared with its condition in earlier stages, so that the value, so computed, is 43.75 per cent. The variability measures prove the variation to be slight, the mean deviation being 5.39 per

TABLE 6

The submucosa and muscularis calculated as 100 per cent, with the mean percentages of its component parts from the sixth fetal month to birth

NUMBER OF CASES	CALCULATED AGE IN FETAL MONTHS	MUSCULARIS MUCOSAE AND SUBMUCOSA	LONGITUDINAL AND OBLIQUE MUSCLE	CIRCULAR MUSCLE	REMAINDER OF MUSCULARIS
2	5.60	17.16	3.74	26.82	52.27
2	6.51	20.87	4.04	37.73	37.34
4	7.50	22.44	4.35	36.48	36.72
4	8.39	25.80	5.43	25.85	42.91
10	9.37	15.77	15.46	30.72	38.03
Mean deviation		0.90	1.23	1.09	1.28
Relative mean deviation		5.71	7.80	3.56	3.38
23	10.37	43.75	8.82	20.01	27.40
Mean deviation		5.39	1.90	3.64	1.46
Relative mean deviation		12.32	21.54	18.19	5.33

cent and the relative mean deviation, 12.32 per cent (table 6). The highly vascular character of the submucosa would make it seem probable that natal hyperemia could be the cause, or at least an influencing factor, of the great relative increase in this lamina.

The weight of the submucosa for 1 sq.cm. of ventriculus wall may be calculated as described in the section on material and methods. For the fetuses of the sixth month the computed weight of the submucosa is 0.015 gram; for the seventh prenatal month, 0.019 gram, and for the eighth lunar month, 0.02 gram. There is a slight drop in this weight for the ninth fetal month, when the figure is 0.017 gram (table 4). At the

tenth fetal month there is evidence of more decrease in the calculated weight of the submucosa, being at that time 0.014 gram, with a mean deviation of 0.002 gram and a relative mean deviation of 16.20 per cent. In the newborn infant the influence of the relative increment in submucosa is reflected in the computed weight of this lamina per square centimeter. At this time the submucosa as calculated weighs 0.050 gram per square centimeter. The mean deviation is 0.009 gram and the relative mean deviation, 18.17 per cent (table 4).

The multiplication of the computed weight of the submucosa in 1 sq.cm. of stomach wall by the surface area of the gastric mucosa in square centimeters gives an estimate of the total amount of submucous tissue in this viscus. This value for the sixth fetal month is 0.141 gram; for the seventh fetal month, 0.351 gram; for the eighth lunar month, 0.467 gram, and for the ninth month of intra-uterine life, 0.459 gram. In the last month of fetal life the submucosa, so computed, weighs 0.519 gram, the mean deviation being 0.108 gram and the relative mean deviation, 20.75 per cent (table 5). By the time of birth the calculated weight of the submucosa has risen to 1.964 grams, with a mean deviation of 0.423 gram and a relative mean deviation of 21.52 per cent.

7. Growth changes of the longitudinal and oblique muscle

The longitudinal and oblique (inner longitudinal lamina) muscle layers are thrown together in the computations made in this study. The oblique fibers are not especially well developed at birth in the region of the stomach from which the samples were taken. Gyllenskoeld ('62) described the early appearance of the inner longitudinal muscle layer in embryos of 91 mm. Welch ('23) found oblique fibers in the stomach of an embryo of 24 mm. This author states that once the oblique fibers are differentiated, they develop very rapidly and in a 33-mm. embryo may be seen in sections almost to the pylorus. He found the oblique fibers in a 65-mm. embryo to form a distinct band, approximately 1.1 mm. in width, at a time when the lateral diameter of the stomach was only 4 mm.

Welch records a gradual increase in oblique fibers from 85 mm. until birth. After birth, there is an accumulation of fibers, especially along the gastric canal. Fleischmann ('75), however, found no oblique muscle fibers at birth. The specimens in the present series show oblique fibers in measurable quantities in all cases. It is true that they are more or less scattered in separate bundles in the earlier fetuses, but at birth a distinct, but very thin, sheet of muscle fibers is present in that region of the stomach which was examined.

The outer longitudinal layer of muscle was clearly defined in all cases, and at birth a very distinct, although somewhat fenestrated, lamina was present. Fischl ('03), however, states that the outer longitudinal muscle is very thin and is entirely absent in places, especially along the greater curvature. Welch ('23) found that the outer muscle layer in later fetal months is "a coarsely fenestrated longitudinal layer, very thin, or absent over the mid-dorsal and mid-ventral portions of the wall."

Expressed in terms of per cent of the total cross-section area of the stomach wall, the longitudinal and oblique muscle laminae have a value of nearly 3 in a fetus of the sixth month. In the seventh prenatal month this value is practically unchanged and at the eighth fetal month is 2.80 per cent. In the ninth fetal month it is 2.66 per cent. The average per cent for the tenth fetal month is 9.26, with a mean deviation of 0.55 per cent and a relative mean deviation of 5.94 per cent. At birth the relative value of these muscle layers has dropped to 6.01 per cent, with a mean deviation of 1.02 per cent and a relative mean deviation of 16.99 per cent (table 1).

When the submucosa and the muscularis are calculated as 100 per cent, the relations of the muscle layers are brought out in a more distinct manner. The longitudinal and oblique muscle, so computed, forms 3.74 per cent of the total at the sixth fetal month. The value rises steadily until the ninth fetal month, when it is 5.43 per cent. In the tenth fetal month the percentage of these layers increases to 15.46, with a mean deviation of 1.23 per cent and a relative mean devia-

tion of 7.80 per cent (table 6). By the time of birth the percentage of longitudinal and oblique muscle has dropped to 8.82, with a mean deviation of 1.90 per cent and a relative mean deviation of 21.54 per cent. This decrease in percentage values at birth is due primarily to the large increase in the submucosa at birth.

When the epithelial and muscle elements are calculated as 100 per cent, as described in the section on surface epithelium, the longitudinal and oblique muscle forms 8.60 per cent of the total in the sixth month of intra-uterine life. There is a slight drop in this relation in the next three fetal months; however, this decrement is not large enough to regard as other than gratuitous variability. In the tenth lunar month the percentage value of these muscle layers is 17.32, with an average deviation of 0.75 per cent and a relative mean deviation of 4.35 per cent (table 3). In the newborn infant the percentage value, so computed, remains materially unchanged, being 16.58, with a mean deviation of 1.64 per cent and a relative mean deviation of 9.89 per cent. When the connective tissues are omitted from the computation, as has been done for the above figures, the relative amount of longitudinal and oblique muscle does not undergo a decrease after it has attained the relation given for the tenth fetal month. This is in keeping with the statements of Baginsky ('82) regarding the precocious muscle development in the stomach in the months immediately preceding birth.

The weight of the longitudinal and oblique muscle laminae may be calculated by methods that have been described in the preceding sections. The computed weight of these laminae for 1 sq.cm. of stomach wall in the sixth fetal month is 0.003 gram; in the seventh and eighth prenatal months the values are the same, being 0.004 gram. In the ninth month of fetal life this weight remains unchanged. By the tenth lunar month the calculated weight of the longitudinal and oblique muscle has increased to 0.014 gram, with a mean deviation of 0.002 gram and a relative mean deviation of 16.09 per cent (table 4). In the newborn infant the computed

weight per square centimeter is 0.010 gram, with a mean deviation of 0.002 gram and a relative mean deviation of 21.75 per cent.

The weight of the longitudinal and oblique muscle laminae may be calculated for the entire stomach by multiplying the figures given in the preceding paragraph by the area of the gastric mucosa in square centimeters. The weights of these laminae, so calculated, are: in the sixth prenatal month, 0.031 gram; in the seventh fetal month, 0.067 gram, and in the eighth fetal month, 0.090 gram. By the ninth fetal month this weight has increased but slightly, if at all. In the tenth month of gestation the longitudinal and oblique muscle layers of the stomach are computed to weigh 0.506 gram. The mean deviation is 0.097 gram and the relative mean deviation, 19.15 per cent (table 5). By the time of birth these laminae are calculated to be 0.387 gram in weight, with a mean deviation of 0.097 gram and a relative mean deviation of 25.04 per cent. The muscle bundles have in this time become more compact and are less scattered. It is entirely possible that this drop in weight may be due to a decrease in the cross-sectional area of the muscle bundles. It is hardly possible that there is any actual loss of muscle fibers.

8. Growth changes of the circular muscle

Lewis ('12) has described the development of the circular muscle layer in the human embryo. He finds this layer complete in an embryo of 22.8 mm. There is an indication, at this time, of a thickening of this lamina toward the pylorus. Fleischmann ('75) has given a description of the condition of the circular muscle at birth. Welch ('23) states that the lamina circularis is well developed at birth and constitutes the greater part of the gastric musculature. He found a marked thickening of the circular layer in the first year of life and accredits this to an interstitial increase.

Relatively, the circular muscle is equal to 21.49 per cent of the cross-section area of the stomach wall in a fetus of the sixth month. In the seventh and eighth prenatal months

this value is higher, being 28.47 and 23.55 per cent, respectively. There is a drop in the next fetal month to one-half of this value. In the tenth fetal month the relative value is 18.45 per cent, the mean deviation being 0.93 per cent and the relative mean deviation, 5.04 per cent (table 1). In the stomach of the newborn infant the circular lamina constitutes 13.83 per cent of the cross-section area of the wall. The mean deviation at this age is 2.55 per cent and the relative mean deviation is 18.46 per cent.

When the submucosa and muscularis are computed as 100 per cent, as described previously, the circular muscle in the sixth prenatal month averages 26.82 per cent. In the seventh and eighth fetal months the percentage value is 37.73 and 36.48, respectively. By the end of the ninth fetal month there is a drop in this relation, the percentage value being 25.85. This decrease is very probably without meaning, for in the subsequent month the circular muscle is 30.72 per cent of the total. The variability is very slight, the average deviation being 1.09 per cent, and the relative mean deviation is 3.56 per cent (table 6). At birth the circular muscle comprises an average of 20.01 per cent of the muscularis and the submucosa. Variability is somewhat greater in the newborn infants than in the series of the last fetal month, the mean deviation being 3.64 per cent and the relative mean deviation, 18.19 per cent. This relative decrease in muscle is partly due to the great increment in the percentage of submucosa, and partly to the condensing of the muscle fibers as has been suggested to be the case in the longitudinal and oblique muscle laminae.

If the epithelial and the muscle elements in the gastric wall be calculated as 100 per cent, the circular muscle in the sixth lunar month comprises 61.73 per cent of the total. In the seventh prenatal month the circular muscle forms 64.02 per cent and, in the eighth month of gestation, 51.25 per cent of the total epithelial and muscle elements. There is a drop of about one-half of this value in the ninth fetal month, for at this time the circular muscle, so computed, is 28.50 per cent. At this time the epithelial elements are at their highest rela-

tive value; this holds particularly true in the case of the glands. The circular muscle in the tenth month of intra-uterine life averages 34.57 per cent when calculated by this method (table 3). In the newborn infant the circular muscle forms 38.57 per cent of the epithelial and muscle parts of the stomach.

The computed weight of the circular muscle in 1 sq.cm. of gastric wall in the sixth fetal month is 0.023 gram. In the seventh prenatal month the calculated weight has increased to 0.035 gram, and in the eighth month of intra-uterine life it is 0.032 gram. The computed weight of circular muscle for the ninth fetal month has dropped to 0.017 gram. In the tenth lunar month this value is 0.028 gram, with an average deviation of 0.005 gram and a relative mean deviation of 17.03 per cent (table 4). In the newborn infant the calculated weight of the circular muscle per square centimeter of the ventriculus wall is 0.023 gram, the mean deviation being 0.004 gram and the relative mean deviation, 17.84 per cent.

The total weight of the circular muscle, calculated as described above, in a fetus of the sixth month is 0.221 gram. By the end of the eighth fetal month the computed weight has increased to 0.761 gram. There is a decrease in the calculated muscle weight in the subsequent fetal month, its value in grams being 0.458. In the last month of intra-uterine life the computed weight of the circular muscle has increased to 1.010 grams. The relative mean deviation is quite large for this series, and it is doubtful if the increase has been as much as the average would indicate (table 5). At birth the calculated weight of the circular muscle is slightly more than 0.9 gram, with a relative mean deviation of 26.82 per cent.

9. Growth changes of the remainder of the tunica muscularis

The remainder of the muscularis may be defined as including the serosa and all other elements, exclusive of the muscle layers, which are found subjacent to the submucosa. As in the case of the remainder of the mucosa, this classification includes areolar tissue, blood and lymph vessels, lymphoid

tissue (when found), and nerves. The muscle bundles are well defined, and in outlining them the septae which break up the larger groups were traced into the bundle as far as possible, the septal tissue being regarded as a part of the remainder of the muscularis.

In the fetuses of the sixth month the remainder of the muscularis averages 41.9 per cent of the total stomach wall as seen in the cross-section. There is a sudden drop in this percentage in the subsequent month, when it is 28.3. From this time until birth the relative value of the remainder of the muscularis is about the same, fluctuating between 23.84 per cent in the eighth prenatal month and 19.02 per cent in the newborn infant. These figures, together with measures of their variability, are found in table 1.

When the submucosa and the muscularis are calculated as 100 per cent, the remainder of the muscularis forms 52.27 per cent of the total in the sixth fetal month. In the following three prenatal months the relative value of the remainder of the muscularis falls between 36.72 and 42.91 per cent. There seems to be no significance in this fluctuation in the material. At the time of birth the percentage value of this part of the stomach wall, so computed, is 27.40. The mean deviation at birth is 1.46 per cent and the relative mean deviation, 5.33 per cent. The figures on which the above paragraph is based are to be found in table 6.

The weight of the remainder of the muscularis may be calculated for 1 sq.cm. of ventriculus wall by the method described in the section on material and methods. This computed weight for the sixth month of fetal life is 0.045 gram; for the seventh prenatal month, 0.034 gram, and for the eighth month of intra-uterine life, 0.032 gram. In the next month the weight of the remainder of the muscularis, so calculated, is 0.023 gram. In the last month of intra-uterine life this value is 0.034 gram, with a mean deviation of 0.006 gram and a relative mean deviation of 17.18 per cent. At birth the calculated weight of the remainder of the muscularis is 0.031 gram, with a mean deviation of 0.003 gram and a relative

mean deviation of 8.50 per cent. The figures on which the above paragraph is based are included in table 4.

The computed weight of the remainder of the muscularis for the entire stomach in the fetuses of the sixth month is 0.430 gram; in the seventh month, 0.609 gram, and in the eighth prenatal month it is 0.760 gram. There is practically no increase in this value in the next month of fetal life. In the fetuses of the last month the remainder of the muscularis, so calculated, weighs 1.254 grams, with a mean deviation of 0.255 gram and a relative mean deviation of 20.37 per cent (table 5). In the newborn infant the computed weight of the remainder of the muscularis for the entire stomach is 1.238 grams and the relative mean deviation is 19.82 per cent.

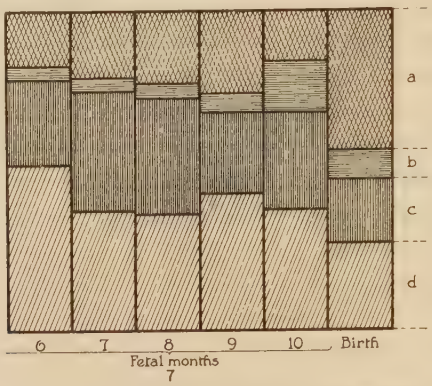
10. Summary of the growth changes of the submucosa and muscularis

The changes in the parts of the muscularis and the submucosa, with relation to the remainder of the stomach wall, are shown graphically in figure 4. This figure shows the relatively enormous increase in the tunica submucosa at birth and the relative decrease in the remaining parts of the laminae subjacent to it. The large relative amount of circular muscle and remainder of the muscularis is also made clear by this figure.

Figure 5 is based upon figures in which the parts of the epithelium—the surface and crypt epithelia and the glands—and the two muscle layers—the inner and outer longitudinal—were calculated as 100 per cent. The circular muscle is shown to form more than 50 per cent of the total in the first three months studied. The inner (oblique) and outer longitudinal muscle laminae are shown to increase relatively when computed in this manner.

When the muscularis and the submucosa are calculated as 100 per cent, the increase in the relative amount of submucosa is more evident than when shown by other methods of computation. This calculation also brings out more clearly the decrease in the relative amount of the circular muscle and

the remainder of the muscularis. The relative amount of inner and outer longitudinal muscle is also shown to be large in the last prenatal month. These findings are presented graphically in figure 7.



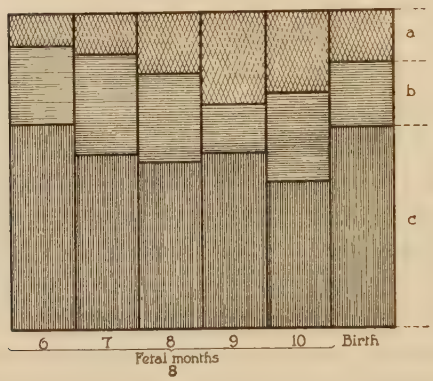


Fig. 7 The percentage values of the parts of the muscularis and submucosa when calculated as 100 per cent, plotted as a histogram from the data in table 6. *a*, muscularis mucosae and submucosa; *b*, longitudinal and oblique muscle; *c*, circular muscle; *d*, remainder of muscularis.

Fig. 8 The mean values of the epithelial, connective-tissue, and muscle elements when calculated as units and figured as percentages of the whole, plotted as a histogram. *a*, epithelial tissue; *b*, muscle; *c*, connective tissue.

11. Growth changes of the epithelial, connective, and muscle tissues

It was thought advisable to ascertain the quantitative relations of these three main types of tissues which are concerned

with the architecture of the stomach wall. To obtain data for the following section, the percentage values, as seen in a cross-section area of the gastric wall, of each of these types of tissues were summated. Into the class epithelial tissue were placed surface epithelium, crypt epithelium, and glands. The connective-tissue class consists of the remainder of the muscularis, the submucosa, and the remainder of the mucosa. The class muscle tissue contains longitudinal and oblique muscle and the circular muscle. The muscularis mucosae is computed with the submucosa because of obvious difficulties in separating it sharply from this lamina in the material at hand. However, it is thought that this discrepancy in classification will not materially influence the figures obtained.

TABLE 7

The mean values of the epithelial, connective-tissue, and muscle elements when calculated as units and figured as percentages of the whole from the sixth fetal month to birth

NUMBER OF CASES	CALCULATED AGE IN FETAL MONTHS	EPITHELIUM	CONNECTIVE TISSUE	MUSCLE
2	5.60	10.33	65.16	24.50
2	6.51	12.95	55.52	31.52
4	7.50	19.64	53.99	23.36
4	8.39	29.12	55.55	15.33
10	9.37	25.71	46.56	27.72
Mean deviation		1.16	1.07	0.63
Relative mean deviation		4.51	2.31	2.26
23	10.37	16.58	63.56	19.86
Mean deviation		3.88	5.31	2.72
Relative mean deviation		23.42	8.35	13.70

a. Epithelial tissue. In the fetuses of the sixth month the epithelial tissue forms 10.33 per cent of the cross-section area of the gastric wall. In the seventh prenatal month this value is 12.95 per cent; in the eighth fetal month, 19.64 per cent, and in the ninth month of intra-uterine life it is 29.12 per cent. For the last fetal month the epithelium averages 25.71 per cent of the cross-section area of the wall of the ventriculus. At the time of birth the epithelium, so calculated, forms but 16.58 per cent of the gastric wall (table 7).

b. Connective tissue. The connective tissues in the sixth fetal month constitute the major portion of the stomach wall, their relative value being 65.16 per cent of the total cross-section area. For the following three fetal months the percentage values are practically the same, ranging from 53.99 to 55.55. In the last fetal month there is a drop in their relative value, being but 46.56 per cent. By the advent of birth the connective tissues are again practically at their value in the sixth fetal month; to be exact, they form 63.56 per cent of the stomach wall as seen in the cross-section (table 7).

c. Muscle tissue. The muscle tissue when computed as a unit shows greater fluctuation than the other types of tissues described above. In the cross-section area of the stomach wall of the specimens of the sixth fetal month, the muscle tissue is 24.5 per cent of the total. In the seventh and eighth fetal months it is 31.52 and 23.36 per cent, respectively. The relative value of the muscle tissue in the ninth prenatal month is 15.33 per cent. The last month of intra-uterine life shows an increase of nearly twofold in this value, and by the time of birth it has dropped to 19.86 per cent (table 7).

TESTS OF METHODS

1. Comparison of the observed and of the calculated weight of the stomach

The weight of the stomach in the fetal period and at birth may be calculated by summating the computed weights of the parts of this viscus for a given age. The calculated weights of the parts of the different stomachs used in this study are presented in table 5. In the sixth prenatal month the calculated weight of the stomach averages 1.02 grams and the observed weight, 1.09 grams. The difference in these two weights, expressed in terms of percentage of the observed weight, is 5.9. The computed weight of the stomach for the subsequent prenatal month is 2.21 grams and the observed weight, 2.07 grams. The difference in observed and computed weights, expressed as percentage of the observed

weight, is 19.4. For the fetuses of the eighth month the mean calculated weight of the ventriculus is 3.22 grams; the observed weight averages 3.74 grams. For the ninth fetal month the calculated weight of the stomach averages 3.62 grams and the mean observed weight is 4.39 grams. The average percentage difference at this age is 16.4. In the tenth fetal month the mean computed stomach weight is 5.47 grams, the average observed weight being 5.61 grams (table 8). The weight of the ventriculus of the newborn infant, when calculated as described above, averages 6.47 grams, while the mean observed weight is less than 0.4 gram greater. The percentage difference at this age is 12.4.

TABLE 8

A comparison of the observed and calculated weights of the stomach from the sixth fetal month to birth

NUMBER OF CASES	MEAN CALCULATED AGE IN FETAL MONTHS	MEAN CALCULATED WEIGHT OF STOMACH	MEAN OBSERVED WEIGHT OF STOMACH	MEAN DIFFERENCE	MEAN DIFFERENCE AS PERCENTAGE OF OBSERVED WEIGHT
2	5.60	1.02	1.09	0.064	5.9
2	6.51	2.21	2.07	0.405	19.4
4	7.50	3.22	3.74	0.456	11.7
4	8.39	3.62	4.39	0.79	16.4
10	9.37	5.47	5.61	0.754	12.9
Mean deviation		1.05	1.14	0.522	
Relative mean deviation		19.18	20.30	69.23	
23	10.37	6.470	6.81	0.851	12.4
Mean deviation		1.020	1.24	0.483	
Relative mean deviation		15.790	18.21	68.460	

The greatest difference in absolute values between observed and calculated weights of the stomach is found in case 10, a newborn infant. In this case the difference is 3.28 grams; however, when this is expressed as a percentage of the observed weight, it is 21.9. In case 5, a newborn infant, the difference is but 1.82 grams; however, this forms 40.4 per cent of the observed weight. The best test of the value of any one of the specimens used is found in the column headed "Difference as percentage of observed weight" in table 8. As a whole, the computed and observed weights of the

stomach check closely in all cases. The highest average percentage difference is found in the series of the seventh fetal month. These figures for the remaining prenatal months fluctuate between 5.9 and 16.4 per cent.

This check of observed and computed weights of the stomachs gives a test of method in three definite instances. It seems to be a reasonable test of the method of obtaining the percentage values of the different parts of the stomach as seen in the cross-section area of the gastric wall. It is apparently a sound test of the manner in which the weights of the various parts were computed. It gives a check on the method used for determining the surface area of the gastric mucosa. The observed weight is in nearly all cases slightly higher than the calculated weight. Since the stomachs were weighed when in 70 per cent alcohol, it seems probable that the difference can be explained by the unavoidable shrinkage due to infiltrating and embedding in paraffin.

2. Other tests of methods

To determine the variability in the percentage values of the parts of the ventriculus wall in the region from which the samples for calculation were taken, an analysis was made of ten different blocks of tissue taken from the same stomach. These pieces of tissue were taken as near as possible to the point where the midsagittal and midtransverse planes of the stomach transect on the ventral surface of this viscus. Case 7, a newborn infant, was selected from the series for this test material. Percentage values of the cross-section areas of these different blocks of tissue were determined by the same technic that was employed in the computations for the other members of the series.

The values for the surface epithelium did not vary more than 1 per cent in any instance. The crypt epithelium is shown to be even less variable than the surface epithelium. The glands are in no instance more variable than 1 per cent. The remainder of the mucosa is almost a constant value. The muscularis mucosae and submucosa vary slightly more than

1 per cent in the ten test samples. The longitudinal and oblique muscle laminae range from 6.12 to 7.06 per cent in relative worth. The circular muscle has a range from 17.03 to 18.05 in percentage value. The remainder of the muscularis was the most variable of all the components of the stomach wall in the test material. The percentage values range from 19.09 to 20.9 for this part.

For a still further test of the method used in deriving the percentage values of the parts of the gastric wall, a number of tracings of the same section were made and the proportions of the parts calculated for each tracing. The test case used was the stomach of a child aged six and one-half years. In all instances the deviation was less than 1 per cent.

SURFACE AREA OF THE GASTRIC MUCOSA

Data on the increase in the surface area of the gastric mucosa in the human are found in the literature only with difficulty. Scammon ('19) has collected and compiled the data of Toldt ('80), Lissenko ('99), and Dargein ('99) on this phase of stomach growth. It is of interest to note that these data, although varying widely in actual figures, follow the same type of curve of growth (Scammon, '19). Scott ('25) has added to these data and presented them in graphic form. With the addition of the present series, there are now available data on this phase of stomach growth from the sixth fetal month to maturity.

The averages of the area of the gastric mucosa in the present series are given in table 9. In the sixth prenatal month

TABLE 9

Weights of 1-sq.cm. blocks of gastric wall and the surface area of the gastric mucosa in square centimeters from the sixth fetal month to birth

NUMBER OF CASES	MEAN CALCULATED AGE IN FETAL MONTHS	MEAN WEIGHT OF 1 SQ.CM. OF GASTRIC WALL IN GRAMS	MEAN SURFACE AREA OF THE GASTRIC MUCOSA IN SQUARE CENTIMETERS
2	5.60	0.106	9.65
2	6.51	0.121	18.16
4	7.50	0.136	23.75
4	8.39	0.134	27.20
10	9.37	0.150	36.93
23	10.37	0.166	39.17

the surface area of the mucosa is 9.65 sq.cm. The mean area of the mucosa has increased in the seventh fetal month to 18.16 sq.cm. In the next month of intra-uterine life this average is 23.75 sq.cm. and in the ninth prenatal month it is 27.20 sq.cm. In the last month of intra-uterine life the mean surface area of the mucosa has increased to 36.93 sq.cm. By the time of birth the surface area of the gastric mucosa is 39.17 sq.cm. These figures coincide quite closely with the areas given in the preceding series (Scott, '25), with the exception of the mean in the series of the tenth prenatal month. The preceding series averaged 32.13 sq.cm. at this age, while the mean surface area in the material at hand is 36.93 sq.cm.

SUMMARY OF FINDINGS

1. The relative amount of surface epithelium seen in a cross-section area of the stomach wall does not change materially when calculated by the methods employed in this study. The computed weight of the surface epithelium per square centimeter of gastric wall increases steadily until the last month of fetal life. There is a slight decrease in this value at birth. The calculated weight of the surface epithelium in the entire stomach increases steadily until the time of birth. Variability measures indicate that the apparent drop in weight of the surface epithelium at birth is probably significant.

2. The relative amount of crypt epithelium, as seen in a cross-section area of the stomach wall, increases steadily until the last fetal month. By the time of birth the relative amount of crypt epithelium has undergone a slight decrease. The calculated weight of the crypt epithelium per square centimeter of gastric wall increases steadily until the last fetal month. In the newborn infant there is a slight decrease in this value. The computed weight of the crypt epithelium for the entire stomach shows a steady increment until the last month of intra-uterine life. By the time of birth this value has dropped about one-third.

3. The relative amount of gland substance, as seen in a cross-section area of the stomach wall, increases until the tenth prenatal month. In the last month of fetal life and at birth there is a progressive decrease in the relative value of the gland substance. At birth the glands form over 30 per cent of the gastric mucosa. The computed weight of the gastric glands, both for 1 sq.cm. of stomach wall and for the entire stomach, follows the same change as does the crypt epithelium.

4. The relative amount of the remainder of the mucosa, as seen in a cross-section area of the stomach wall, increases steadily until the close of the ninth fetal month. In the last prenatal month and at birth the percentage of the remainder of the mucosa decreases. The computed weight of the remainder of the mucosa for 1 sq.cm. of stomach wall shows a steady increase until the tenth fetal month. This value remains practically constant. The calculated weight of the remainder of the mucosa in the entire stomach shows a steady increase with the advance in fetal age.

5. The relative amount of submucosa, as seen in a cross-section area of the stomach wall, fluctuates considerably until the time of birth. At birth the submucosa forms nearly one-third of the gastric wall. The computed weight of the submucosa in 1 sq.cm. of stomach wall follows roughly the same change as does the relative amount of this lamina. The calculated total weight of submucosa in the stomach shows a steady increase until the last fetal month. In the newborn infant there is an enormous increase in this weight.

6. The inner (oblique) and outer longitudinal muscle laminae, when calculated as percentage of the total cross-section area of the stomach wall, show no great changes until the tenth fetal month, when there is an enormous increase of about three times their former value. In the newborn infant there is a decrease from this high relative value. The computed weight per square centimeter of stomach wall follows the same growth change as does the relative value. This is also true for the total calculated weight of these laminae.

7. The lamina circularis gives evidence of a general decrease in relative value when computed as a percentage of the total cross-section area of the gastric wall. The calculated weight of the circular muscle per square centimeter of stomach wall shows considerable fluctuation. The total calculated weight of circular muscle is at the highest value in the tenth fetal month.

8. The relative amount of the remainder of the muscularis seen in a cross-section area of the gastric wall shows considerable fluctuation, but there is evidence of a decrease by the time of birth. The computed weight per square centimeter of the remainder of the muscularis shows the same change as does the relative amount. The total calculated weight of this part of the stomach wall shows an increase with fetal age.

9. The epithelial tissues, as a whole, undergo a rapid increase in relative amount from six to nine fetal months. There is a decrease in the relative value of these tissues from this time until birth.

10. The muscle tissues, as a whole, show a slight increase and then a decrease in relative value until the last month of fetal life, when there is a marked increment. In the newborn infant there is again a marked decrease in their relative value.

11. The connective tissues undergo a relative decrease during the fetal period and a later increase in relative value at birth.

12. The surface area of the gastric mucosa, as determined in this study, shows a steady increment with the advance in fetal age.

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